"The master of disaster prose" —The Nation

# THE MONSTER ENTERS

COVID-19, Avian Flu and the Plagues of Capitalism

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## "Mike Davis's *The Monster* . . . gives me everything that the news cycle doesn't: a sense of the interconnected forces and the history that set us up for what we're experiencing."

#### —Molly Dektar, *Vogue*

Ith this expanded and revised version of his earlier book, *The Monster at Our Door*, renowned activist and author Mike Davis brings an unsparing eye to bear on the COVID-19 pandemic now sweeping the world. He sets the current crisis in the context of previous viral catastrophes, notably the 1918 influenza disaster that, in just three months, killed at least forty million people, and the Avian flu of a decade and a half ago that sounded a tocsin, disastrously ignored by those in power, for today's devastating outbreak.

In language both accessible and authoritative, *The Monster Enters* surveys the scientific and political roots of today's viral apocalypse. Along the way it exposes the key roles of agribusiness and the fast-food industries, abetted by corrupt governments and a capitalist global system careening out of control, in creating the ecological pre-conditions for a plague that has brought much of human existence to a juddering halt.





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COVID-19, AVIAN FLU, AND THE PLAGUES OF CAPITALISM

#### MIKE DAVIS



#### New York · London

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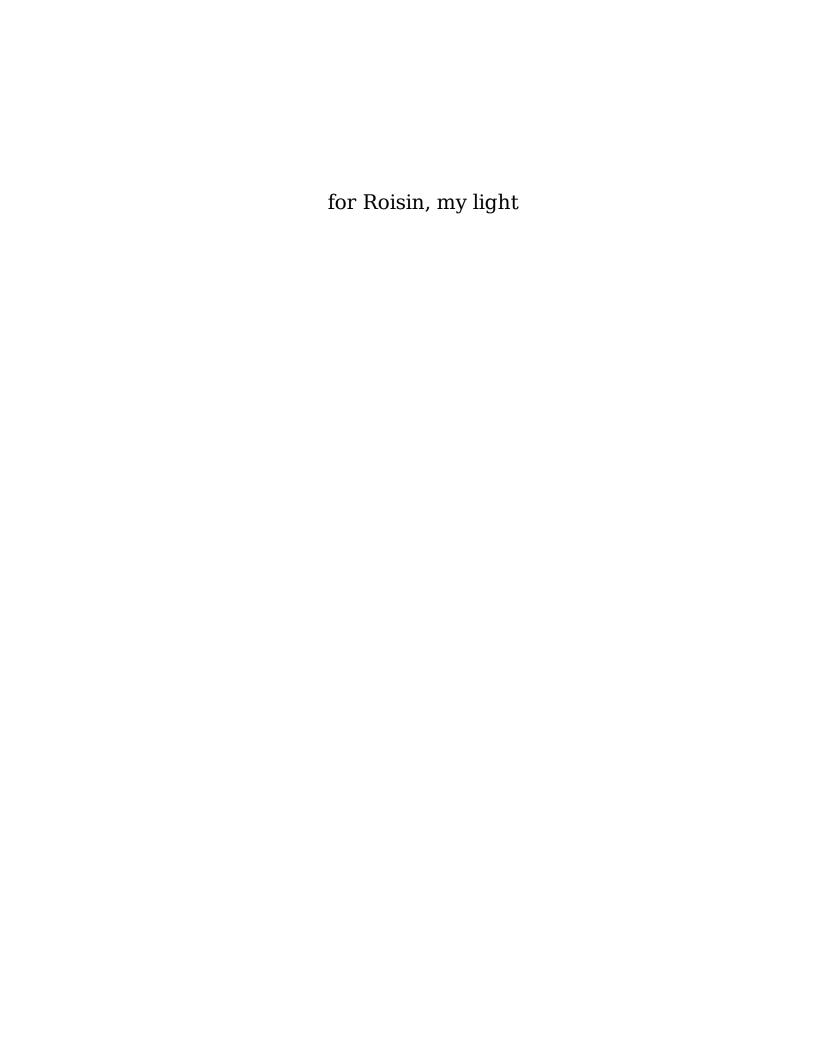
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Lo, when the wall is fallen shall it not be said unto you, Where is the daubing wherewith ye have daubed it? Ezekiel (xiii, 3, 10-12)

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#### INTRODUCTION: THE MONSTER ENTERS

I write this in the first week of April 2020, in the eye of the hurricane, so to speak, while bunkered in my garage with innumerable cans of Chef Boyardee, a few pints of Guinness, and some virology textbooks. A few weeks ago I bought *The Monster at Our Door* online, since I had long ago given away all my copies. Unconsciously, I suppose, I wanted it off my bookshelf in order to exorcise the anxiety involved in its writing. But the threat of a planetary pandemic—most likely avian flu—remained very much on my melancholy Celtic mind, along with the ghost of my mother's little brother, a victim of the Spanish flu in 1918, whom she still lamented decades later.

But today we are locked nervously in our homes like the poor denizens of London in Daniel Defoe's *Journal of the Plague Year* thanks to an obscure virus that escaped from a bat and showed up in one of the world's megacities. The emergence of SARS-CoV-2, the coronavirus that causes COVID-19, wasn't entirely surprising. Its older sister, SARS-CoV, had already scared the pants off the world back in 2003, and another deadly iteration, MERS, emerged in Saudi Arabia in 2012 and has killed almost 1,000 people. But coronaviruses, in the opinion of most scientists, were a team at the bottom of the emergent virus league,

overshadowed by heavy hitters like H5N1 (avian flu), Ebola, and even the Zika virus.

The pandemic, according to my current publishers, has given new relevance to my old flu *Monster*, most of which is reprinted here. I should emphasize, however, that the threat of an avian flu outbreak and its global spread continues to be "imminent." The original flu monster, H5N1, now has even deadlier avian siblings— H7N9 and H9N2— and as the World Health Organization (WHO) warns, flu viruses have a "vast silent reservoir in aquatic birds" and "are impossible to eradicate." <sup>1</sup>

Moreover, as Rob Wallace has shown in a brilliant book, the factory farming of poultry for fast-food outlets has become a diabolic incubator and distributor of new flu types.<sup>2</sup> Given the inevitability of flu pandemics, the development of a universal flu vaccine that provides multiyear immunity against all subtypes of influenza A must be given the highest priority, despite disinterest by bottomliners in the pharmaceutical industry.<sup>3</sup>

SARS-CoV-2, meanwhile, flies across the globe influenza-like wings: unexpected a high rate of transmissibility magnified by the number of invisible spreaders—that is to say, contagious people without easily recognizable symptoms. It also kills by viral and bacterial pneumonia in the same way as influenza. Because of these similarities, a generation of work modeling the likely dynamics and geography of an avian flu pandemic is now an invaluable resource in the battle against COVID-19. But the current virus and its mother genus, Coronaviridae, differ radically in some respects from the influenzas and indeed

all other RNA viruses. Let's take a closer look at SARS-CoV-2.

#### **CORONAVIRUSES: DEADLY ECLIPSES**

Viruses, which are likely responsible for 90 percent of infectious diseases, are basically parasitic genes that hijack the genetic machinery of the cells they invade to make myriad copies of themselves. The small group of viruses based on DNA have a built-in proofreading mechanism to ensure accurate replication, but viruses programmed by RNA like influenzas and coronaviruses lack it. As a consequence, some species are like bizarre Xerox machines running at ultra-high speeds that constantly spit out errorridden copies. As a recent article in *The New England* Journal of Medicine observes: "It took the genome of the human species 8 million years to evolve by 1%. Many animal RNA viruses can evolve by more than 1% in a matter of days." By producing so many inaccurate versions of their genomes such viruses have a huge advantage in resisting the human immune system because inevitably there will arise copies at least partly resistant to the antibodies produced in past infections or generated by vaccination.

Viruses—particles smaller than bacteria that easily passed through porcelain filters—were for decades the great enigmas of early modern microbiology. They were first imaged in the late 1930s, shortly after the invention of the electron microscope. Scientists were stunned by their wild array of different structures and forms. For example, influenza A—a wilder, more dangerous viral genera than influenzas B or C, which cause common colds and winter

flus—looks like a naval mine (a sphere with studded spikes). The viruses that infect bacteria look like tiny Mars landers and Ebola, like a worm. The *Coronaviridae*, discovered in 1937, are tiny solar eclipses. In a photomicrograph their protruding "petals"—S proteins that allow the virus to latch onto a cell surface—definitely give the appearance of the solar corona during a total eclipse. Thus the name of the family.<sup>5</sup>

Coronaviruses are unusual in several respects: in the first place because their genome, a single twisted helix inside a protein capsule, is the largest RNA molecule in nature. "Nucleotides" are the structural building blocks of DNA and RNA genomes. Influenza A viruses have 14,000 packaged in eight separate segments, coding for ten to fourteen proteins. Coronaviruses, on the other hand, have 30,000 nucleotides. Like influenza A, they also have two principal modes of evolution. The accumulation of small mutations inevitably sprouts new strains or subtypes. This process is known as *antigenic drift*.6

Far more dramatic—standing in the same relationship to drift as revolution does to reform—is *antigenic shift*. If an animal or human cell is simultaneously infected by two different influenza viruses, say one from a wild bird and the other a human-transmitted strain, replication can shuffle the genomic deck. Lethal segments from the wild flu can end up packaged together with segments from a flu already circulated among people that has the key for unlocking human cells. Pertinent to understanding the rest of this book, the molecules often traded in these *reassortments* are species-specific hemagglutinins (HA), the unique keys used

by viruses to open host cells, and neuraminidase (NA), the escape artists that help new viruses break out of the infected cell's membrane for further spread—hence the influenza subtype formula, HxNy. As I requested in the original *Monster*, "Please remember this. It will avoid confusion later on when you meet a series of bad characters named H3N2, H9N1, H5N1, and so on." Virologists speculate that such "'reassorted" types that combine virulence with ease of infection are responsible for the flu pandemics that erupted in 1890, 1918, 1957, 1968, and 2009. The "Spanish flu" that infected fully half of the human race, however, was two orders of magnitude more deadly than the others: two percent mortality versus .02 percent.

A second unusual characteristic of coronaviruses is they are even more adept shape-shifters than orthomyxoviruses like influenza A. Because their genome is a single, unsegmented strand, they can't reshuffle the deck in the same manner as influenza does through repackaging separate segments of different strains. But what they accomplish is even more amazing: *recombination*, "the splicing of different parts of genes (coding for the same protein) from different species." To quote from a standard virology textbook:

Coronavirus RNA genomes undergo a high frequency of recombination, as high as 25% for the entire coronavirus genome. This is noteworthy since the nonsegmented genomes of most other RNA viruses display levels of recombination ranging from low to undetectable.

The ability of coronaviruses to recombine at high frequency, together with their high mutation rate (which is a property of all RNA viruses), may also enable them to adapt to new hosts and ecological niches more readily than other RNA viruses. Recombination can also occur between

different coronavirus strains, providing additional opportunities for these viruses to adapt to new niches. 8

Before the emergence of SARS in 2002-3 (the subject of chapter four) coronaviruses were mostly of interest to veterinary science. Although two recognized human strains were believed to cause 10 to 20 percent of colds (human rhinoviruses are the major culprit), most research was focused on deadly outbreaks among pigs, cattle, turkeys and other domestic animals, especially their young. $\frac{9}{2}$ Porcine Epidemic Diarrhea Virus, first identified in China in 1971, killed millions of piglets and cast a permanent shadow over pork production. In the 1990s another coronavirus, Bovine CoV, was shown to be the cause of several lethal cattle diseases, including the mysterious "Shipping Fever." In such cases giant feedlots and factory pig farming, where the extreme stress of confinement wrecks animals' immune systems, undoubtedly accelerated the emergence of new coronavirus types as well as their growing capacity for interspecies transmission. 10

SARS coincided with a recurrence of avian flu (the first major outbreak had occurred in Hong Kong in 1997), with which it was initially confused. No one suspected it was caused by a coronavirus and this resulted in a flood of misinformation from major research centers. Eventually a crack team of researchers at the University of Hong Kong isolated and cultured a novel pathogen that turned out to be a previously unknown coronavirus, *SARS-CoV*. (In dishonorable fashion, the U.S. Centers for Disease Control and Prevention [CDC] tried to claim credit for the discovery

but were rebuffed by the international research community.) $\frac{11}{2}$ 

Unlike the animal coronaviruses, or for that matter the Spanish flu, SARS generally spared the young while killing half of infected elderly patients. It had a variable incubation period, from four days to two weeks, but only became transmissible when people were symptomatic. For this reason, the epidemic was suppressed after the adoption of comprehensive testing, contact tracing, and isolation of cases. With HIV (a retrovirus) still slaughtering hundreds of thousands of Africans in the background, SARS sounded the alarm that a new viral pandemic was nigh, one that threatened everyone regardless of their sexual mores or needle use. As Estair Van Wagner wrote in a collection of essays on SARS, global networks, and world cities:

SARS has made it impossible to guarantee that the borderless enclave of the identical hotels, condos, office buildings, and convention centers that facilitate the mobility of the transnational elite is disease free. In the face of a possible avian influenza outbreak ... the presumption that our governance and health infrastructure have either the knowledge or power to control infectious diseases is no longer tenable and appears dangerously arrogant. 12

As bird flu cases grew in 2004–5, H5N1 reclaimed the stage and the White House Homeland Security Council rushed out a National Strategy for Pandemic Influenza, complemented by a Department of Health and Human Services (HHS) report on implementation of measures. Other reports and updates (the latest in 2017) further specified investments that urgently needed to be made in detection, testing, vaccine development, protection of

critical infrastructure, and so on.<sup>13</sup> Likewise the WHO in 2005 created an Emergency Committee, which updated its guidelines for member governments and defined their international responsibilities in such an outbreak. SARS was demoted, although it had achieved pandemic status, because it lacked flu's deadly ability to be spread by asymptomatic and pre-symptomatic individuals. Meanwhile, Ebola viruses (there are four in humans) augured an alternative biological apocalypse. Ebola disease disseminates quickly and had an early kill rate of 90 percent in some localities. Pandemic researchers were soon modeling scenarios for its spread outside Africa.

Then in 2012 the Curse of Tutankhamun struck Saudi Arabia: a new SARS-like disease caused by a coronavirus resident in Egyptian tomb bats and transmitted to humans via infected dromedary camels and perhaps by goats. Middle East Respiratory Syndrome (MERS), as it was baptized, was subsequently contracted by a Korean visitor and produced a small outbreak in South Korea. 14 By 2017 some 2,000 cases had been reported with a death rate (36 percent) inching toward Ebola levels. But the great majority of patients had had contact with infected animals and in the minority of cases where human-to-human transmission occurred, it involved intimate contact with people already displaying the symptoms. This indicates, say scientists, that MERS has been unable to fully adapt to human transmission. On the other hand, they were startled by its unexpected talent for easily crossing species boundaries. 15

A group of scientists in Texas quickly advanced research on a MERS vaccine, but it excited minimal interest. Earlier they had successfully developed a SARS vaccine but couldn't find a corporate or government sponsor interested in testing and manufacturing it. The lead researcher, Dr. Peter Hotez, dean of the National School of Tropical Medicine at Baylor University, told the House Committee on Science in early March that he believed the vaccine, which has been sitting in a freezer for years, might have provided cross-protection against COVID if it had been available in quantity and tested in the field during the first month of the outbreak. "There is a problem with the ecosystem in vaccine development, and we've got to fix this." 16

But MERS did spur successful research on coronaviruses in bats. SARS investigators in 2003 had quickly identified civets—small, catlike carnivores that are consumed, ironically, because they are believed by traditional practitioners to cure flu—as the immediate carriers of the disease; then in 2005 they found bats with SARS-CoV and realized that they were the likely source of the infection in civets, the intermediate host. Gradually the hypothesis that bats were the natural reservoir for many if not all coronaviruses became a framework for new investigations. The research discoveries since 2012 have revealed the astonishing genetic diversity of coronavirus strains circulating in different bat species. A recent audit of these studies by a team in Wuhan concluded:

From 55 published articles on bat coronaviruses at the time of preparation for this book chapter, more than 102 bat species from around the world have been shown to carry coronaviruses. Currently,

eight bat coronaviruses have been classified as species, but more than one hundred bat coronaviruses (or strains) have not yet been classified. However, as there are more than 1200 bat species in the world, large numbers of new bat coronaviruses likely await discovery. 17

Other studies indicate a large number of virulent bat viruses, capable of infecting humans, also circulate in pig populations where they have caused repeated epidemics. Given the huge, unsuspected size of these coronavirus reservoirs, SARS-CoV-2's long leap from bats to pangolins to humans should not have been surprising. And it probably wasn't to the virologists researching bats. But it was an earthquake to epidemiologists and public officials who, influenza or Ebola pandemic, expecting an concentrated their efforts on antivirals and vaccines for those diseases. "The emergence and rapid spread of COVID-19," wrote two international experts, "signifies a perfect epidemiological storm. A respiratory pathogen of relatively high virulence from a virus family that has an unusual knack of jumping species boundaries, that emerged in a major population center and travel hub shortly before the biggest travel period of the year: the Chinese Spring Festival."18

It will be some time before the evolution of SARS-CoV-2 is retraced, and it may have been a "cryptic spread" among humans before the first cluster of pneumonia cases was detected in Wuhan.  $^{19}$  It's not yet known whether it is the product of *drift* or *shift* or a complex combination of the two processes.  $^{20}$  Like avian flu and SARS, it erupted out of a Chinese live animal or "wet market," presumably from a stall selling pangolins, the scaly anteaters that are

occasional menu items. (China's failure after SARS to ban the sale of exotic animals, including bats, in food markets is both puzzling and disastrous, although the trade is now banned.)<sup>21</sup> The pangolin—or whatever animal was the intermediate host—was infected by a bat and SARSCoV-2 may be a mutated version of the same precursor bat virus that was responsible for SARS. Indeed, Australian researchers report that 96 percent of the SARS-CoV-2 genome is shared with a virus found in horseshoe bats. This may be the mother of both viruses.

COVID-19 has some striking similarities to SARS and MERS. First, they present almost identical symptoms at the outset: fever, dry cough, and aching muscles. All three cause high mortality via pneumonia and sepsis among the aged and those with immune-compromised bodies. In each case the virus is also shed in feces, and because the lining of the small intestine has similar receptors to those of the respiratory system, fecal-oral infection is possible. It remains unknown what degree of immunity is conferred on survivors of these three diseases, but, using coronavirus colds as an analogue, it is probably short-lived, perhaps only a year. So COVID is most likely here to stay as a chronic disease.

But the new virus is signally different from SARS and MERS in at least three respects. First and most importantly is its ability to be spread in a flu-like manner by people who lack recognizable symptoms. (To repeat, the transmission of both SARS and MERS has been by visibly sick people or animals.) Second, it appears to infect heart tissue, and *Kaiser Health News* reports that doctors are starting to see

coronary damage in one out of five hospitalized. Apart from those who die directly from heart attacks, a small number at present, the legacy of the pandemic could be permanent heart problems for thousands of survivors. Third, as researchers recently discovered, it is one hell of a tough nut:

SARS-CoV-2 is very strange with one of the hardest protective outer shell ... among coronaviruses. This means that it might be expected to be highly resilient in saliva or other body fluids and outside the body. An infected body is likelier to shed greater numbers viral particles since the latter is more resistant to antimicrobial enzymes in body fluids. These particles are also likelier to remain active longer. These factors could account for the greater contagiousness of the SARS-CoV-2 and have implications for efforts to prevent its spread. 23

Although not as deadly as SARS or MERS, COVID-19's currently guesstimated 2 percent mortality rate is comparable to the Spanish flu, and like that monster it probably has the ability to infect a majority of the human race unless antiviral and vaccine development quickly come to the rescue. Even if future studies based on blood sampling for evidence of COVID-19 antibodies reveal a far greater number of positive cases than now modeled, thus significantly reducing the death rate, the earth's population is now four times larger than in 1918 and the ultimate hecatomb could still be counted in millions.

#### SHOUTING INTO WASHINGTON'S VOID

"So it's really as bad as that," said Miranda.

"It's as bad as anything can be," said Adam, "all the theaters and nearly all the shops and restaurants are closed, and the streets have been full of funerals all day and ambulances all night."  $^{24}$ 

In this celebrated short novel written twenty years after the event, Katherine Ann Porter recorded her own near-death experience during the Spanish flu pandemic of 1918–19. She spent nine days in the hallway of an overwhelmed Denver hospital, burning with fever, drifting in and out of hallucinations. Her lover, a young lieutenant awaiting orders to leave for France, lay elsewhere, dying. Shivering on her steel gurney and given up as hopeless by her doctor, Miranda/Ann sees phantoms, soldiers, and executioners hovering over an "old man in filthy clothes":

The road to death is a long march beset with all evils and the heart fails little by little at each new terror, the bones rebel at each step, the mind sets up its own bitter resistance and to what end? The barriers sink one by one, and no covering of the eyes shuts out the landscape of disaster, nor the sight of crimes committed there.

In 1918–19, despite enormous recent advances built upon the fundamental discoveries of Koch and Pasteur a generation earlier, medical science was almost as helpless in the face of the pandemic as had been the physicians, alche-mists and astrologers called upon to cure the Great Plague of 1665–66 in London. If the U.S. Public Health Service wagered everything on the distribution of an ultimately worthless vaccine, the remedy in Daniel Defoe's time was to slaughter all the cats in the city—a great windfall for infected rats. In both eras medicine chased phantoms: the plague bacillus was finally identified by Alexandra Yersin in 1894, while a full characterization of the 1918 virus waited until 2000, when an expedition brought back the frozen lungs of an original victim from the Arctic.

Today's "landscape of disaster" is eerily similar to 1665 and 1918: urban populations locked inside their apartments, the flight of rich to their country homes, the cancelation of public events and schools, desperate trips to the markets that often end with infection; society's reliance upon hero nurses, the lack of beds in hospitals and pest-houses, the mad search for masks, and the widespread suspicion that alien powers are at work (Jews, a passing comet, German saboteurs, the Chinese).

But this time around there was little mystery about the identity of the microbe—SARS-CoV-2 was sequenced almost overnight in January—or the steps necessary to fight it. Since the discovery of the HIV virus in 1983 and the recognition that it had jumped from apes to humans, science has been on high alert against the appearance of deadly new diseases with pandemic potential that have crossed over from wild fauna. This new age of plagues, like previous pandemic epochs, is directly the result of economic globalization. The Black Death, for instance, was the inadvertent consequence of the Mongol conquest of inner Eurasia, which allowed Chinese rodents to hitchhike along the trade routes from northern China to Central Europe and the Mediterranean. Today, as was the case when I wrote *Monster* fifteen years ago, multinational capital has been the driver of disease evolution through the burning or logging out of tropical forests, the proliferation of factory farming, the explosive growth of slums and concomitantly of "informal employment," and the failure of pharmaceutical industry to find profit in the

producing lifeline antivirals, new-generation antibiotics, and universal vaccines.

Forest destruction, whether by multinationals desperate subsistence farmers, eliminates the barrier between human populations and the reclusive wild viruses endemic to birds, bats, and mammals. Factory farms and giant feedlots act as huge incubators of novel viruses while appalling sanitary conditions in slums produce populations that are both densely packed and immune compromised. The inability of global capitalism to create jobs in the socalled "developing world" means that a billion or more subsistence workers (the "informal proletariat") lack an employer link to healthcare or the income to purchase treatment from the private sector, leaving them dependent upon collapsing public hospitals systems, if they even exist. Permanent bio-protection against new plagues, accordingly, would require more than vaccines. It would need the suppression of these "structures of disease emergence" through revolutionary reforms in agriculture and urban living that no large capitalist or state-capitalist country would ever willingly undertake. A cadre of brilliant medical researchers, public-health doctors, and informed journalists —Paul Farmer, Richard Horton, Laurie Garrett, Rob Wallace, and many others—have been trying to teach us for about these systemic connections. As Wallace emphasized a few years ago, "the agroeconomic impacts of global neoliberalism are foundational, felt across biocultural organization, down so far as the virion and molecule."26

A much larger chorus of voices, many shouting from the highest rooftops of government, have warned that a

catastrophe such as the one that we are now living through loomed on the horizon and perhaps was imminent. The successive debuts of avian flu (1997, 2003-present), SARS (2003), Swine flu (2009), MERS (2012), and Zika virus (2015), as well as the recent Ebola epidemics in the Congo and West Africa, produced surges of research and attracted smart biotech start-ups who tried, often unsuccessfully, to find venture capital to back the development of promising new antivirals and vaccines. The specter of avian flu, as I mentioned earlier, had led to the adoption of an official U.S. national strategy and the emergence of a new genre of scientific literature: report after report warning of a coming pandemic and the need to prepare to meet it.

preparedness stop-and-go was a cycle politicians often backtracked from their own policies. In 1998, for instance, the Clinton administration created a National Pharmaceutical Stockpile under CDC management expressly to deal with the pandemic threat. In 2003 the Bush administration changed the name to the National Strategic Stockpile and handed control over to Homeland Security (DHS) and HHS. Its inventory then included 105 million N-95 respirators, 100 million of which were distributed by the Obama administration during the swine flu (H1N1) emergency in 2009. The Obama administration, however, failed to replenish the mask stockpile, arguing that a better and cheaper solution was to help the private sector develop the production capacity to meet surging demand in a pandemic crisis. Trump's DHS and HHS officials, many of whom were political appointees with little experience in public health administration or even medical science, were content to leave the stockpile depleted while neglecting the proposed investments in private-sector alternatives.

Trump also scrapped the hard-earned wisdom of those who had fought previous major outbreaks. Following the terrifying Ebola outbreak in West Africa in 2014, field reports and analyses from a number of different U.S. agencies were synthesized in a memorandum by NSA analyst Christopher Kirchhoff and sent to Susan Rice, Obama's national security advisor. After the combined forces of the WHO and various medical nonprofits failed to contain the initial outbreak, the CDC, USAID, and other U.S. agencies attempted to fill the gap, but their own lack of coordination only produced more chaos. Finally, considering the outbreak a tier-one national security emergency comparable to the civil war in Syria, President Obama established a White House Ebola Task Force and mobilized the Pentagon, who, in inimitable fashion, conceptualized their mission as the equivalent to fighting terrorists. In the end 2,800 troops were sent to Liberia to build laboratories, hospitals and barracks for the hundreds of U.S. Public Health Service's doctors and lab workers.

The sobering lesson learned from this experience, Kirchhoff concluded, was that "gaps in preparedness and capacity surfaced in every major agency tasked with health and security in the U.S." (He later told an interviewer that "Those of us in the Ebola response knew we got lucky, not only because the pathogen wasn't airborne, but because the outbreak happened where it did in the world. We knew that we probably wouldn't get lucky again.") Kirchhoff

made a case for a whole spectrum of reforms, but stressed that only "a single person accountable to the President for response efforts, working within the NSC framework, is a model that works in *extremis* cases." Rice and Obama agreed and the Directorate of Global Health Security and Biodefense was created inside the National Security Council with the specific responsibility of monitoring and advising the executive branch about the pandemic threats. Its first "czar" was Beth Cameron, a State Department veteran who reported directly to Rice. 27

The directorate survived the change of regimes, but in 2018, when John Bolton became Trump's third National Security Advisor, he told his leader that there was no need for a separate pandemic group and that it was more efficient to fold its work into a single NSC center for weapons of mass destruction and biowarfare. He started by purging a counterpart pandemic planning group in DHS, then in a night of long knives, closed the NSC directorate and fired most of its staff, starting with its head, Rear Admiral Timothy Ziemer. Bolton's ruthless destruction of the two directorates evoked a storm of protest from medical experts and former Bush and Obama officials. The Center for Strategic and International Studies took up their case and convened a commission that included Julie Gerberding, the head of the CDC during the George W. Bush years, and Kelly Ayotte, a former Republican senator from New Hampshire. Just weeks before the outbreak they published a report "sounding the alarm that the U.S. government is caught in a cycle of crisis and complacency" in regard to

preparing for a pandemic. The first step, they urged, was restoring expert health leadership on the NSC.<sup>28</sup>

At almost the same time, a report from the Council of Economic Advisors (CEA) warned that existing vaccine production technologies were out of date and incapable of meeting needs during a pandemic. With incredible prescience they forecast that a pandemic could incapacitate a large portion of the workforce, require the hospitalization of as many as 4.3 million people, and kill half a million. Pondering the failure of the pharmaceutical industry to modernize vaccine development, they offered a compelling explanation that any radical economist would likely agree with:

There is a key misalignment between the social and private returns from medical research and development and capital investment in pandemic vaccines. R&D and investment costs are only recouped by sales when the pandemic risk occurs. Part of the value of vaccines that can mitigate future pandemic risks, however, is their insurance value today that provides protection against possible damage. This insurance value accrues even if the pandemic does not occur in the future, and it implies that the social value of faster production and better vaccines is much larger than its private return to developers. This divergence leads to an under-provision in vaccine innovation because it does not get rewarded for its insurance value. Second, pandemics represent a risk with a small probability of occurring but with large and highly correlated losses across the population. The rarity of influenza pandemics and the fact that the last serious one in this country occurred a hundred years ago may lead consumers and insurers to underestimate the probability and potential impact of a future influenza pandemic. Moreover the risk cannot be effectively pooled because evervone is at risk concurrently. 29

This analysis, of course, applies with equal force to the reluctance of Big Pharma to develop new antibiotics and antivirals, as well as to the insurance industry's refusal to provide pandemic insurance.

But in the blizzard of warnings and dire predictions in the two years before the pandemic, there were also some rays of sunshine. Thus at the beginning of 2018, lead researchers at the Vaccine Research Center of the National Institutes of Health heralded a revolution in vaccine design based on recent advances in next generation sequencing, rapid monoclonal antibody recognition, the application of AI to biological design, and atomic-scale protein engineering. making these "fast vaccines," the researchers explained, would require a new scale of investment and international collaboration, plus an expanded network of observatories in areas of high biodiversity where animalhuman transmission is most likely. The following year researchers from the Center announced that the holy grail was in sight: "As a result of these advances, high-level, broad, and durable immunity against the large universe of influenza viruses may now be within reach."30 Meanwhile Halyard Health, a firm commissioned by the Obama administration three years earlier to update the technology of N-95 mask manufacture, had succeeded by fall 2018 in building a prototype machine that could produce 1.5 million masks per day, ten times the current industry maximum. This would meet the surge demand for masks in a pandemic as correctly foreseen and calculated by Obama's HHS.31

"Fast vaccines," a universal flu shot, high-speed mask production—bells should have rang out, but they didn't. The mask technology bore the fatal stamp of an Obama program —all of which Trump had vowed to drive a silver stake through—and the other breakthroughs involved the kind of urgent science-driven investments that most Republicans frowned upon in the same way as they derided clean energy and universal health care. In any event, the administration was preoccupied with more urgent health-related issues such as junking Obamacare and kicking more than one million people off food stamps. The CDC also came under the knife and its global health section "was so drastically cut in 2018 that much of its staff was laid off and the number of countries it was working in was reduced from 49 to merely 10." A parallel attempt to eliminate the \$252 million that Obama had committed to rebuilding health systems in three Ebola-ravaged countries was ultimately blocked by Congress. 32

And just three months before the Wuhan outbreak, it axed funding for USAID's Emerging Pandemic Threats PREDICT program, which had been established after the avian flu scare in 2005. A highly lauded pet project of both the Bush and Obama administrations, PREDICT was both a pioneer viral early warning system and an aid program training local medical professionals to recognize novel infections and monitor zoonoses (animal outbreaks) that might be transmitted to humans. Its ultimate goal was the preemption of future pandemics through identification and surveillance of dangerous viruses. According to Science, PREDICT over the years had "discovered more than 1000 viruses from viral families that contain zoonoses, including viruses involved in recent outbreaks, and others of ongoing public health concern." This total included 160 potentially dangerous corona-viruses identified in bats and other

animals. (The total size of the global reservoir of animal viruses with the potential to become human infections is vastly greater. The Global Virome Project, a major international collaboration, estimates that there are 1.6 million unknown viruses circulating in wild animals, half of which have zoonotic potential.)<sup>33</sup>

#### THE APOCALYPSE IN SIX EASY STEPS

Nobody knew there would be a pandemic or epidemic of this proportion. Nobody has ever seen anything like this before.

President Donald Trump, March 16, 2020

Someday—if and when we emerge from our pandemic fallout shelters—diligent journalists will reconstruct in detail Trump's craven abdications, tantrums, lies, and sundry high crimes and misdemeanors during this crisis. For now, it is possible to summarize the major factors responsible for the catastrophic meltdown of the federal response in the first three months of the pandemic.

First, there was no continuity of leadership experience from the Obama era or even from the first two years of Trump's presidency. In the last days of the Obama White House, the president's homeland security advisor, Lisa Monaco, invited her incoming counterpart, Tom Bossert, to co-organize a large-scale test of the country's preparedness to deal with a viral pandemic. She was concerned whether the lessons were passed on to the Trump Cabinet and agency heads. "Crimson Contagion," which took place just a week before the Inauguration, was coordinated by HHS with the participation of a dozen federal agencies and twelve states. Its storyline supposed that an avian flu

outbreak in China was brought back to the United States by tourists. The exercise revealed innumerable problems arising from the friction of competing agencies and officials as well as the cacophony of demands from governors and mayors. "But the problems," according to a *New York Times* investigation, "were larger than bureaucratic snags. The United States, the organizers realized, did not have the means to quickly manufacture more essential medical equipment, supplies or medicines, including antiviral medications, needles, syringes, N95 respirators ventilators, the agency concluded." Among the participants from the new administration, in addition to Bossert, were Rex Tillerson, John F. Kelly, and Rick Perry, all of whom reportedly accepted the lessons of the simulation. The White House did not, and by 2019 all of the leaders who took part in Crimson Contagion, as well as the author of the CEA report, had either resigned or been fired. The Trump administration is its own fifth column. 34

Second is the shocking incompetence and poor judgment of the CDC, which declined the use of the coronavirus test kit developed for the WHO by a German firm. It has been the consensus of experts internationally that the immediate response priority in a pandemic is widespread testing, contact tracing and isolation of positive cases. This has been done successfully in South Korea, Germany, Singapore, and Taiwan, as well as in China following the fatal mistakes in January that forced the total closure of Wuhan. All these countries had quickly produced ample stockpiles of WHO-type test kits. The CDC, on the other hand, opted to design its own test kit, which it unveiled on January 24. But the

third stage component of the test was flawed and gave false results. The entire month of February was thus wasted while the CDC tinkered with the kit rather than switching to the available WHO design. (The use of an alternative test kit developed by Stanford scientists at the beginning of the month was blocked by FDA red tape.) "Had the United States," concluded an investigation by the *New York Times*, "been able to track its earliest movements and identify hidden hot spots, local quarantines might have confined the disease." 35

The same disaster may be repeating itself in the case of a blood test for immunity, a procedure that could certify which people can safely return to work. Germany is preparing to conduct trial tests, hoping it will allow its specialized metallurgical industries to roar back to life and revive its lucrative exports to China. Other countries in Europe and Asia are not far behind Germany. "The U.S., by according to comparison," a LosAngeles investigation, "hasn't come up with a coherent plan for large-scale antibody testing, which health experts say could dash chances for a return to public life and leave health officials with few options for managing the pandemic other than severe social restrictions until a vaccine or drug therapy is available."36 Such a delay would have the most dire consequences for an economy already plunging into a 1932-like depression.

Third, the "stay at home" and "social distancing" strategy is a second-best approach made necessary by the failure to implement early testing and detection. Indeed "flattening the curve" is a poor substitute for preventing its

exponential increase in the first place. As a last resort measure, it requires immediate and comprehensive implementation, but Trump fiddled and stalled, leaving it to Democratic governors and mayors to try to put out the fire. Even as the president was compelled by public opinion to limited grudgingly application of approve quarantines and then a widespread shutdown of nonessential workplaces, hardcore red-state governors (eight at time of writing) have resisted shutdowns with the same zeal as their predecessors resisted racial integration. They have been co-conspirators in a viral spread that is bound to take tens of thousands of lives, especially in the Deep South.

Ground zero for the outbreak in the region was the Mardi Gras at the end of February that attracted a million celebrants. This was a bit like the masked ball in Poe's Mask of the Red Death and the dancers were not all wearing red. According to the Washington Post, "New Orleans Mayor LaToya Cantrell [a Democrat] said canceling or curtailing Mardi Gras was never considered. Federal agencies that are part of planning Mardi Gras every year—including the FBI and Homeland Security—did not raise concerns about the coronavirus, she said. Federal officials who walked the parade route with members of her administration were focused on terrorist attacks." Most of the visitors were from other parts of Louisiana and neighboring states and returned home with the virus to seed outbreaks in smaller towns and cities lacking the laboratories, ICU nurses, and ventilators to treat COVID. The regional medical centers in larger cities like New Orleans, Baton Rouge, and Jackson

(Mississippi) that normally play that role are now overwhelmed and unable to accept critical cases from their rural peripheries.

Fourth, all the competent responses in other countries had ample inventories of personal protective gear-N-95 masks, gowns, and goggles—available to assure the safety of firefighters, postal workers, bus drivers, and police, as well as medical staff. Especially in East Asia, the world center for the production of such supplies, the use of surgical masks by the general public during flu season is an old custom, and it was an easy step to require that everyone going outside their home wear a mask. In contrast, the United States provides a catastrophic counterexample. Nothing I think better symbolizes state failure than the fact that on the same day that Trump was making his usual boasts about the country's unparalleled scientific and technological might, the New York Times devoted a full page to "how to sew your own mask." Millions of Americans are now doing so, in the absence of products that cost mere pennies to manufacture. The shortages of N-95 masks, as well as throat swabs and testing reagents, come at an incalculable cost in the wake of the test kit fiasco. Countries that had all these essentials available not only saved thousands of lives, but were able to safely maintain essential parts of the economy.

Despite the fact that the Korean War-era Defense Production Act is invoked thousands of times each year by the Defense Department to ensure that contractors meet their deadlines, the Trump White House, cheered on by the U.S. Chamber of Commerce, has refused to use it to accelerate the manufacture of these lifeline products. (The revolutionary Halyard Health mask machine meanwhile gathers dust.) This fatal decision to rely on the president's rapport with corporate leaders rather than nationalize production as in wartime goes hand in hand with the break in precedent of putting Mike Pence and Jared Kushner in charge of the response over continuing the tradition of letting the CDC coordinate the mobilization with the aid of a uniformed logistics expert from the Department of Defense. The result is Katrina writ a hundred or even a thousand times larger.

Fifth, the now-depleted National Strategic Stockpile was created to allow Washington to directly aid stricken cities and regions in a health emergency. Kushner's recent assertion that mandate was only to supplement state inventories is a blatant falsehood, designed to pass the buck and rationalize the White House's refusal to take decisive leadership in addressing all the shortages and production bottlenecks. Although the Trump administration has been a power grab in almost every sense, it has consistently rejected power's responsibilities. Thus the Trump Doctrine: states and cities should forage on their own for ventilators and protective supplies. As Maryland's ex-governor Martin O'Malley caustically observed, "that is а Darwinian approach to federalism; that is states' rights taken to a deadly extreme."38

Moreover, Trump's oft-repeated claim that most states had access to abundant medical resources is the opposite of the actual case. Across the country, the 2008 recession had been a bloodbath for local health departments, trimming

their workforces by a quarter and closing a dozen major public-health laboratories. The loss of experienced public health nurses in particular has come back to haunt many localities. Fiscal austerity also became a pretext for reducing or eliminating states' own emergency medical stockpiles. The blame, as the case of California illustrates, falls on both parties. In response to the threatened 2005 avian flu pandemic, Governor Arnold Schwarzenegger and the Democratic leaders of the legislature spent hundreds of millions of dollars to stockpile 2,400 portable ventilators, 50 million respirators, and materials to assemble 21,000 additional hospital beds. They also invested in three stateof-the-art 200-bed mobile hospitals that could be up and running within 72 hours of a disaster. But Schwarzenegger was succeeded by a notorious penny pincher named Jerry Brown, who in 2011 crossed out the annual allocation of \$5.8 million to maintain the stockpile. While the state's chief medical officer and others wept, the strategic supplies hospitals, specifically mandated for viral field emergencies like COVID-19, were either given away or sold off. $\frac{39}{}$ 

Six, Trump's CDC, still reeling from the test kit fiasco, has abdicated a principal role in vaccine development as have Big Pharma and the WHO. Within the White House, moreover, there has been no visible enthusiasm for the kind of public "moon shot" effort that so many scientists deem necessary. Instead the leadership vacuum has been filled by the Coalition for Epidemic Preparedness Innovation (CEPI), a nonprofit headquartered in Oslo that was launched three years ago by the Gates Foundation, the Wellcome Trust, and

the governments of Norway, Germany, and Japan. Led by Richard Hackett, one of the principal authors of the 2005 National Strategy for Pandemic Influenza, the CEPI funnels investment to ambitious startups and small-to-medium-sized firms that it believes have the talent to advance innovations like mRNA technology and now a vaccine for SARS-CoV-2. The research community it funds has become a hothouse where molecular biologists and biotechnologists, in an ever-expanding global collaboration, are sharing ideas with astonishing speed and openness as they struggle to move candidate antivirals and vaccines to the testing stage. 40

But CEPI and similar collaborations do not have the funding to accelerate the transition from the laboratory to production line. A COVID vaccine, it is estimated, would require an investment of at least \$2 billion to roll out the tens of millions of vaccinations that are required just to cover the elderly and chronically ill. In an editorial for Science, Seth Berkley, another longtime crusader for vaccine research, set parameters for what was immediately needed: "If ever there was a case for a coordinated global vaccine development effort using a 'big science' approach, it is now."41 Such a viral Manhattan Project would require at least three things: dynamic U.S.-China cooperation such as existed during the Ebola epidemic, 42 direct government funding and production of the vaccine and other life-saving drugs (an idea endorsed by Senator Elizabeth Warren), and world-class scientific leadership at the helm. From a Trumpian perspective, however, you might call those the "three anathemas."

#### THE SCREAMING STREETS

Social distancing is a privilege.

It means you live in a house large enough to practice it.

Hand washing is a privileged too. It means you have access to running water.

Hand sanitisers are a privilege. It means you have money to buy them.

Lockdowns are a privilege. It means you can afford to be at home.

Most of the ways to ward off Corona are accessible only to the affluent.

In essence, a disease that was spread by the rich, as they flew around the globe will now kill millions of the poor. $\frac{43}{}$ 

Dr. Jagadish J. Hiremath

In Defoe's Journal of the Plague Year, one of the most disquieting images is that of a poor street, its doomed residents locked inside their slum tenements, screaming. Whether these "incessant roarings" came from victims' agonies (the later stages of plague are incredibly painful) or were the wails of mothers over their dead children, or children over their dead mothers, was impossible to distinguish. But all of London screamed for eighteen months.

It seems inescapable that the great sickly slums of Africa and South Asia—Khayelitsha, Kibera, Dharavi, Makoko, and so on—will soon be screaming. Up until now, the coronavirus infections in East Asia, Europe, and North America have been only marginally more deadly than the flu among healthy, well-fed people under 50. But immunologically there are two distinct humanities. In the first, only the elderly and chronically ill have been led up the pyramid steps to be sacrificed to COVID-19. In the other, where malnutrition, disease, and contaminated water compromise the immune systems of people of all ages and respiratory ailments are legion, the carnage is likely to

become more widespread and indifferent to demography. Poverty, density, and hunger, in other words, will likely reshape the pandemic.

To take the case of Africa first, 237 million of its sub-Saharan population are chronically undernourished and half of the deaths of young children are the result of hunger. Moreover, UNICEF has recently warned that the number of children under five who show evidence of stunted growth has been increasing by millions over the last twenty years. (This is why we must distrust the claim that since the population of Africa is the world's youngest, with over-65s comprising only 3 percent of the population—versus 23 percent in Italy—the pandemic would pass over without great mortality.) Malnutrition, like chronic illness, becomes deadly when coupled with severe viral infections.

The history of the Spanish flu teaches a grim lesson about the co-morbidity of hunger and infection. Almost 60 percent of global mortality (that's at least 20 million deaths) in 1918–19 occurred in the Punjab, Bombay, and other parts of western India, where grain exports to Britain and brutal requisitioning practices coincided with a major drought. Resultant food shortages drove millions of poor people to the edge of starvation. They became victims of the sinister synergy between malnutrition—which suppressed their immune response to infection—and rampant bacterial, as well as viral, pneumonia. In a similar case, British-occupied Iran, several years of drought, cholera, and food shortages, followed by a widespread malaria outbreak, preconditioned the death of an estimated one-fifth of the population. (See chapter one.)

In addition to hunger, COVID-19 in Africa will feed on a host of other vulnerabilities. HIV/AIDS has killed 36 million Africans over the past generation and researchers estimate that there are currently 24 million cases, alongside millions suffering from the "white plague"—tuberculosis. Throttled by neocolonial debt since the 1980s and by a quarter century of wildly destructive civil wars in west and central Africa, much of the continent's medical infrastructure is in ruins and five of the six nations judged to have the world's worst health care are in Africa. One of them is Nigeria, where medical treatment for 206 million people is now almost entirely privatized and beyond the reach of the poor. 45 With exception of South Africa, moreover, none have the existing capacity to treat more than a handful of critical COVID-19 cases. Kenya, a country well-known for exporting nurses and doctors, has exactly 130 ICU beds and 200 certified ICU nurses to treat 50 million people. Sudan, with a similar population, has but 30 beds.

Without local public health "fire departments," the recent Ebola outbreaks quickly grew into firestorms that were only put out with massive international aid. The United States alone spent \$6 billion to build emergency hospitals from scratch in the affected countries. Japan and China also provided major assistance. This time around, with South Africa and Ethiopia in the leadership, the whole continent is crying out simultaneously for medical aid as well as debt relief for their sinking economies. But the response from the big guns of Europe, North America, and Japan, as well as the IMF and World Bank, has been tepid at best. China, whose interest in Africa might be described as

quasi-imperialist, has rushed to fill the vacuum, but the vast demand for medical aid exceeds its capacities. As for Washington, "America First" means "Africa Last." To date, even the progressive wing of the Democratic Party has remained silent about our responsibility to aid Africa.

There's also some possibility that mass infection in slums and poor countrysides could flip a switch on coronavirus's mode of infection. In the veterinarian research mentioned earlier that looked at coronavirus epidemics among domestic animals, the investigators discovered two different routes of infection: fecal-oral, which attacked stomach and intestinal tissue; and respiratory, which attacked lungs. In the first case there was usually very high mortality, while the second generally resulted in milder cases. Multiple studies confirm that SARS-CoV-2 is being shed copiously in feces and accumulated in sewage. 46 In African and South Asian slums, of course, fecal contamination is everywhere: in the water, in homegrown vegetables and as windblown dust. (Yes, shit storms are real.) In addition, most of Africa's slum communities are built in low-lying areas that flood during the rainy season. Raw sewage, often in open ditches, then spreads everywhere, even into homes. All of this favors the enteric route and raises the question of whether, as in the case of animals, this will lead to more lethal infections, possibly across all age groups?

### **LESSONS FROM WUHAN**

A recent article in the journal *Infection* discusses the reasons behind China's apparent success in suppressing the first wave of COVID-19. Although public authorities in

Wuhan initially tried to cover up the outbreak and censor the press, once Beijing realized the scale of infection and the rapidity of its spread, it moved aggressively. The draconian quarantine of Wuhan and nearby cities along national travel restrictions dramatically slowed transmission to the rest of China. This allowed thousands of doctors, nurses, and emergency personnel from all over China to pour into Hubei, where construction crews were building huge emergency hospitals literally overnight. Initial shortages of test kits, respirators, and protective quickly overcome as the were government aggressively ramped up their production.

According to Chinese reports, corroborated by the WHO, the number of cases has been held to under 1 million out of the 57 million population of Hebei: an attack rate of only 2 percent, much lower than expected. By contrast, Governor Newsom recently wrote to President Trump that California's experts are predicting a population infection rate of 56 percent (25.5 million cases) over the next eight weeks.

It is, of course, the case that as China relaxes the quarantine and sends workers back to offices and factories the infection could come roaring back, in the absence of a vaccine. There are warning signs that this may already be occurring as Chinese citizens bring the infection back from Italy and other hot spots. The three Asian countries that like China have suppressed local outbreaks—Taiwan, Singapore, and South Korea—face the same threat. Thus the return to work is a controlled experiment and all four countries are well aware that they may have to quickly slam on the

brakes again, albeit with further damage to their economies.

Trump's inner circle, whose envy of China is limitless, claimed for much of March that they too would soon relight the boilers and return people to work by Easter. The president's cheerleaders at Fox News started chanting "the cure is worse than the disease" while the Republican Party's king of fools, Texas lieutenant governor Dan Patrick, bravely volunteered to sacrifice the elderly to COVID if necessary to keep the economy generating profits. Having lost control over the pandemic, they seemed to be seriously weighing achieving herd immunity by putting a large portion of the workforce in its path while the Fed printed money to revive Wall Street. It was an idea with almost Hitlerian overtones that Trump grudgingly retreated from after Anthony Fauci scoffed at it.<sup>48</sup> It also signaled to Beijing that Washington was in complete disarray.

Western reaction to China's management of the crisis veered between discordant stereotypes. During the early weeks in Wuhan local leaders conformed to the image of a corrupt bureaucracy with wooden legs. (Something very happened 2003.) But the similar had in massive intervention of the central government and the rapid extinction of outbreaks in other parts of China was widely attributed to the efficient power of a quasi-totalitarian surveillance state. Both perceptions were in some part true, but they tell only part of the story. As Republican senator Bill Cassidy of Louisiana, a senior gastroenterologist, emphasized meanwhile Trump accused Chinese president Xi Jinping of engineering a cover-up: Chinese medical

scientists have been "outstanding" in quickly sharing crucial information with the world medical community. Indeed, their constant stream of reports and statistics has become the informational foundation for doctors and researchers everywhere.

At the same time, China and Cuba are the only countries currently rising to the challenge of providing significant medical aid and expertise to poorer nations. Cuba's internationalist doctors have for decades been the first on the scene of dangerous outbreaks in the Third World, suffering heavy casualties in recent battles against Ebola in West Africa. They are the reliable shock troops, but the Chinese bring in the heavy artillery—a promised conveyor belt of medical experts, test kits, protective gear, and so on. While Italy's European sisters, in what may be the death blow to the European project, close their borders and refuse to share supplies, China is preparing a massive medical rescue operation in loose coordination with Russia. Most tellingly, Chinese foundations have sent New York a thousand of the vital ventilators that Trump has failed to deliver.

Beijing, of course, is playing hegemonic politics and burnishing its image at a time when Washington has placed a "stay away and don't call" sign on the Statue of Liberty, and the WHO is crippled by the inaction of the big Western governments. The Trump regime, meanwhile, acts in character: continuing to build its border wall despite the health risk to workers, cutting off vital medical aid to north Yemen in the midst of a famine, doubling down its economic blockades of Cuba and Iran, and turning a blind eye to the

imminent disaster in Africa. But to an ordinary Liberian farmer or Kenyan mother, or for that matter an elderly Italian locked inside an apartment, what matters are not promises but masks, medicine, and lots of doctors' boots on the ground.

In recognizing China's achievements, however, we should avoid learning the wrong lesson: state capacity for decisive action in an emergency does not necessitate the suppression of democracy. Despite what many talking heads are claiming, putting a million Uighurs in reeducation camps was not a precondition for quelling the coronavirus in Hubei, nor has the Big Brother practice of surveilling all the jaywalkers in Chinese cities and scoring their "social credit" proved essential to the success of the national quarantine. Certainly the Communist Party's pervasive presence in daily life—90.6 million members organized into thousands of workplace and neighborhood committees was a decisive factor in the total mobilization against COVID, but this mainly confirms the critical importance of grassroots organization and preparedness, necessity of a police state. Repression, although used viciously against the original heroic whistleblowers in Wuhan—now "disappeared"—has otherwise played little role in China's success.

Still it's inevitable that the rightwing leaders in the White House, Downing Street, Beit Aghion, and elsewhere will seize every opportunity, as they did with 9/11, to appropriate new authoritarian powers, exploiting the consequences of their own inaction and disastrous leadership to set more precedents for closing public spaces,

banning assemblies, and even suspending elections. A case in point has been Israeli prime minister Benjamin Netanyahu's use of the emergency to hobble parliamentary assemblies and let Shin Bet, the country's internal security service, tap everyone's phones. In Hungary, another "coronavirus coup" has given President Viktor Orban the power to rule by decree without a time limit, as well as to muzzle the opposition press. Thus dictatorship returns to Europe for the first time since the death of Franco.

That's why we need to be debating democratic models of effective response to present and future plagues, ones that mobilize popular courage, put science in command, and use the resources of a comprehensive system of universal health coverage and public medicine. Otherwise we cede leadership in this age of constant emergency to our tyrants.

# PREFACE: THE MONSTER AT OUR DOOR

The evil that happened here in the last month was a  $sign.\frac{1}{2}$ 

The village chief of Ban Srisomboon

In a time of plague, like the influenza pandemic that swept away my mother's little brother and 40 to 100 million other people in 1918, it is difficult to retain a clear image of individual suffering. Great epidemics, like world wars and famines, massify death into species-level events beyond our emotional comprehension. The afflicted, as a result, die their physical agonies are redoubled by the twice: submergence of their personalities in the black water of megatragedy. As Camus put it, "a dead man has no substance unless one has actually seen him dead; a hundred million corpses broadcast through history are no more than a puff of smoke in the imagination."<sup>2</sup> No one mourns a multitude or keens at the graveside of an abstraction. Unlike certain other social animals, we have no collective sorrow instinct or biological solidarity that is automatically aroused by the destruction of our fellow kind. Indeed, at our worst we find a perverse, often delectable sublimity in Black Deaths, tsunamis, massacres, genocides, and collapsing skyscrapers. In order to grieve over a cataclysm, we must first personify it. The Final Solution, for example, has little gut impact until one reads *The Diary of Anne Frank* or sees the pitiful artifacts in the Holocaust Museum. Then it is possible to weep.

The threat of avian influenza—a plague-in-the-making that the World Health Organization (WHO) fears could kill as many as 100 million people in the next few years—is perhaps most movingly exemplified by the story of Pranee Thongchan and her daughter Sakuntala. Indeed, the image of the dying eleven-year-old tenderly cradled in the arms of her young mother was the *pieta* that gave visceral meaning to the writing of this little book, which reports on the failure of our government and others to protect the world from the imminent danger of an almost unfathomably dangerous influenza outbreak. The intimate and heartmoving scale of this mother-daughter tragedy is precisely what will be lost if avian flu, as so many predict, becomes the next great pestilence of globalization, following in the wake of HIV/AIDS.

Ban Srisomboon is a village of 400 households in Thailand's northern province of Kamphaeng Phet, a pleasant, sleepy region whose decayed temples and palaces attract few tourists but which is renown throughout the country for its famous bananas. Like rural Thais elsewhere, the people of Ban Srisomboon are preoccupied with chickens. They raise free-range poultry for cash income, then invest their earnings in the fighting cocks that are a national obsession. In late August 2004, however, chickens started dying mysteriously throughout the village, much like the rats in Oran in the early scenes of *The Plague*.

Unlike the hapless *colons* in Camus's famous novel, however, the farmers of Ban Srisomboon recognized that the dead chickens were a portent of the avian influenza that had been insidiously creeping across Thailand since November 2003.

Given the genetic license-plate number "H5N1" by virologists, this flu subtype had been first recognized in Hong Kong in 1997 when it jumped from waterfowl to humans, killing six of its eighteen victims. A desperate cull of all the poultry in the city contained the first outbreak, but the virus simply went underground, most likely in the "silent reservoir" of domestic ducks. In 2003, it suddenly reappeared on an epic scale throughout China and Southeast Asia. Researchers were horrified to discover that H5N1—like the doomsday bug in Michael Crichton's old The Andromeda thriller. Strain—was becoming "progressively more pathogenic" both to chickens and humans. In the first three months of 2004, as new human fatalities were reported from Vietnam and Thailand, more than 120 million chickens and ducks were destroyed in a massive international effort to create a firebreak around the outbreak. Most of the slaughtered poultry belonged to small farmers or contract growers who were often wiped out by the losses.

The family heads of Ban Srisomboon thus faced an excruciating dilemma. On one hand, they were aware that the disease was truly dangerous to their children as well as their chickens and that they were legally required to summon the authorities. On the other hand, they also knew that the government would promptly kill all their poultry,

including their prized fighting cocks. The official compensation was only 20 *baht* per bird (about 50 cents), but the cocks were worth up to 10,000 *baht*—in some cases, they were a family's principal wealth.<sup>3</sup>

Bangkok newspapers reported different versions of how the village resolved this contradiction. In one account, the villagers decided to hide the outbreak and hope for the best. In another version, they twice warned the Agriculture Ministry that abnormal numbers of chickens were dying, but officials failed to inspect the village. In any event Sakuntala's uncle, Somsak Laemphakwan, later told reporters that he dug deep holes to ensure that his dead birds did not spread their infection. Despite this precaution, his niece, who like other village children had daily contact with the birds, soon developed a suspicious stomachache and fever. Somsak took her to a nearby clinic, but the nurse dismissed her illness as a bad cold. Five days later, however, Sakuntala began to vomit blood, and she was rushed to the district hospital in the town of Kamphaeng Phet (population 25,000). When she continued to deteriorate, her aunt, Pranom Thongchan, called Sakuntala's mother, who was working in a garment factory near Bangkok, and told her to come home quickly.4

Pranee was horrified to discover her daughter in the terminal phase of viral pneumonia: coughing up blood and gasping for breath (pneumonia kills by slow suffocation). Throughout that last night, according to nurses, she cradled her daughter, kissing and caressing her, whispering endearments; such love, one hopes, would have allayed some of the little girl's terror and suffering. (The accounts

were especially poignant to me as they early recalled my mother's recollection—she was eight in 1918—of the death of her toddler brother in the arms of her stepmother.)

The hospital listed Sakuntala's cause of death as "dengue fever" and she was cremated before anyone could take a tissue sample. At the funeral, Pranee complained of muscle aches and acute exhaustion, and her family took her to the same clinic that had misdiagnosed her daughter's critical illness as a cold. In a dreadful repeat of the earlier incompetence, Pranee was reassured that she was just suffering from grief and exhaustion. She returned to her factory job, but she soon collapsed and was rushed to a hospital where she died on September 20, two weeks after her daughter. She was only twenty-six years old.

While public health officials awaited an autopsy report on Pranee, her sister, Pranom, was in medical isolation with similar symptoms. Fortunately, the doctors now suspected bird flu and quickly administered a course of oseltamivir (Tamiflu), a powerful antiviral that, if administered promptly, has proven uniquely effective against the most deadly strains of influenza. While Pranom was recovering, teams of men wearing gas masks and white biosafety suits nervously entered Ban Srisomboon, now a "red zone," to kill, bag, and bury all the remaining birds. Other crews in rubber boots and rain gear sprayed disinfectant on "everything from pickup trucks full of schoolboys to threewheeled tractors." In an atmosphere of near panic, villagers avoided their neighbors but, at the first sign of a cough or sniffles, raced into the district hospital emergency room, terrified that they had the bird plague.

Their fears were not irrational: on September 28, the WHO announced that Pranee had probably contracted her infection directly from Sakuntala, thus marking the first person-to-person transmission of avian flu since the emergence of the current virulent subtype in 1997. Although the WHO and the Thai government tried to downplay the significance of Pranee's death—"a viral dead end" in the words of one official—influenza researchers knew that the disclosure deserved the headlines and alarm it generated around the world. If the avian virus had acquired enabling genes from a human influenza strain, then Pranee might be only the first of millions of new victims of a plague that in its current incarnation (poultry-to-human transmissions) was killing two-thirds of those it infected.

The essence of the avian flu threat, as we shall see, is that a mutant influenza of nightmarish virulence— evolved and now entrenched in ecological niches recently created by global agro-capitalism—is searching for the new gene or two that will enable it to travel at pandemic velocity through a densely urbanized and mostly poor humanity. This is a destiny, moreover, that we have largely forced upon influenza. Human-induced environmental shocks tourism, wetland destruction, overseas a corporate "Livestock Revolution," and Third World urbanization with the attendant growth of megaslums—are responsible for turning influenza's extraordinary Darwinian mutability into one of the most dangerous biological forces on our besieged planet. Likewise, our terrifying vulnerability to this and other emergent diseases has been shaped by concentrated urban poverty, the neglect of vaccine development by a pharmaceutical industry that finds infectious diseases "unprofitable," and the deterioration, even collapse, of public-health infrastructures in some rich, as well as poor, countries. The evil that visited Ban Srisomboon, in other words, was not some ancient plague awakened from dormancy, if such can exist independent of historical circumstance, but a new form in whose creation we have inadvertently but decisively intervened. And that, as the villagers in Ban Srisomboon avowed, is surely a "sign."

## CHAPTER 1: THE VIRULENCE OF POVERTY

Our worst nightmare may not be a new one.<sup>1</sup>
Richard Webby and Robert Webster

Influenza is both familiar and unknown. Although easily distinguished from most common colds by a characteristic moderate to high fever and dry cough, influenza A can exhibit an extremely broad range of symptoms (including sore throat, headache, bone aches, conjunctivitis, dizziness, vomiting, and diarrhea) that overlap with numerous other so-called "grippes, catarrhs and colds." The continuing, rampant prescription of antibiotics for influenza is proof of the difficulty that most general practitioners and clinic staff face in distinguishing between viral and bacterial infections. "[I]t is now accepted," writes one world authority, "that influenza is quite protean in its manifestations. Influenza cannot be distinguished readily on clinical grounds from other acute respiratory infections, and during virologically proportion confirmed outbreaks of influenza the influenzal illnesses confirmed by laboratory tests as being influenza is currently about half."2

If diagnosis is often mere guesswork, an accurate census of influenza mortality is almost an impossibility: except during pandemics, influenza is usually only the accessory to murder. By destroying the ciliated epithelial cells that sweep dust and germs out of the respiratory tract, flu superinfection by bacteria. (Haemophilus encourages influenzae—widely believed in 1918-19 to be the actual pathogen of the pandemic—is a famous fellow traveler.) A lethal synergy is believed to operate between influenza A and pneumonic bacteria, with Staphylococcus aureus and Strepto coccus pneumoniae being particularly vicious; thus, bacterial pneumonia is the most common, or at least the most clearly associated cause of influenza deaths. But how to distinguish influenza-related cases from the rest of pneumonia mortality? As Registrar General of England William Farr first realized during an influenza epidemic in 1847, the infection's well-defined seasonality (October to March in the Northern Hemisphere) in temperate countries allows a rough calculation of excess mortality by simple subtraction of the annual average from the winter spike.<sup>3</sup>

Although epidemiologists now use sophisticated regression modeling, influenza mortality is still estimated in North America and Europe as excess annual mortality. it has become evident that the Recently, however, traditional reporting category "pneumonia and influenza" shortchanges influenza's deadly impact. Most of the winter disease. spike heart in ischemic diabetes. cerebrovascular disease mortality may also result from the impact of the annual flu epidemic; conversely, "influenza vaccination has been associated with large reductions in the risks of primary cardiac arrest, recurrent myocardial infection, cardiac disease and stroke." In a normal year, researchers now believe that influenza kills between 36,000

to 50,000 mostly elderly (and especially poor) Americans, a reality that belies the benign image of flu as nothing more than a winter nuisance. Sadly, an infection that primarily kills infants and old people is not likely to arouse as much concern as a disease that kills young or middle-aged adults.

As difficult as it is to estimate flu mortality in this country, global influenza mortality is mere conjecture. "There is," writes one research team, "an underappreciation and an underestimation of the impact of influenza in the developing world." It is sometimes said that flu kills 1 million people worldwide each year, but the toll could be considerably higher because annual influenza is the least recognized of all so-called "captains of death." Neither China nor India, for instance, reports flu statistics to the World Health Organization. In tropical countries, moreover, the absence of well-defined seasonality in the incidence of influenza makes estimation of excess mortality difficult. This dearth of data, in turn, has reinforced the stereotype that there is no significant influenza burden in Asia or Africa.

While high death rates from acute respiratory infections in the tropics are often attributed to tuberculosis, recent research has established that a majority of acute respiratory deaths are caused by viruses, and that tropical countries have influenza mortality rates at least equivalent to those in the mid-latitudes. Indeed, "infection probably has an even greater relative impact on the health of persons from developing countries who are of underlying complications because susceptible to malnutrition, tropical diseases and HIV." Moreover, infant

mortality from influenza is probably considerably higher in low-income tropical countries. 9

Influenza is most of all a mystery disease in sub-Saharan Africa. The region is the weakest link in the global influenza-surveillance network coordinated by the WHO: in recent years Côte d'Ivoire, Zambia, and Zimbabwe have closed down their national flu surveillance systems after pleading debt and bankruptcy; currently only South Africa and Senegal actively track flu cases and have the laboratory resources to isolate and characterize subtypes. In the rest of Africa, serious flu cases are commonly conflated with malaria or just added to the "acute respiratory infection" (ARI) grab bag. Yet annual influenza in Africa does often produce explosive local outbreaks, such as the 2002 epidemic in Madagascar, which overwhelmed the country's health care system, or the massive irruption six months later in the Equateur Province of the Democratic Republic of the Congo, which yielded shocking rates of secondary pneumonia. 10

Third World influenza is also largely invisible or poorly studied in the historical record. The apocalyptic pandemic of 1918–19—according to the WHO, "the most deadly disease event in the history of humanity"—is the template for the public-health community's worst fears about the imminent threat of avian influenza. After two generations of cultural amnesia, popular interest in the history and legacy of the "Spanish flu" (so called because uncensored newspapers in neutral Spain were the first to report its arrival) has undergone a dramatic revival in recent years.

The threat of a new pandemic, meanwhile, spurs continuing research into many aspects of the 1918 virus's molecular structure; the enigmatic circumstances of its emergence (reassortment or recombination?), its geographical origin (a Kansas army base, the trenches in France, and southern China are all proposed epicenters), 12 and its distinctive mode of attack (which produced singularly high mortality among young adults). Despite renewed scholarly investigation into the 1918 pandemic, however, shockingly little attention has been paid to the disease's ecology in its major theater of mortality in 1918–19: British India.

Table 1: Pandemic Mortality 1918–19—Revised 13

Worldwide	(a) 21.64 million	(b) Asia 48.8 to
		100 million
Asia	15.78	26 to 36
India	12.50	18.5
China		4 to 9.5
East Indies	.80	1.5
Europe	2.16	2.3
Africa	1.35	2.38
W. Hem.	1.40	1.54
USA	.55	.68

(a) Jordan (1927); (b) Johnson & Mueller (2002)

The enormity of influenza's impact on India has never been questioned. For decades the authoritative guide to

worldwide pandemic mortality was the 1927 American Medical Association-sponsored study—*Epidemic Influenza* —by Edwin Oakes Jordan, editor of the prestigious *Journal* of Infectious Disease, who had spent years poring over death statistics. The huge spike in mortality during the fall of 1918—U.S. life expectancy fell by ten years—allowed him to make estimates of the pandemic toll despite the absence of influenza data per se (see <u>Table 1</u>). Jordan believed that global mortality from influenza was in the range of 20 to 22 million (about 1 percent of the human race), with India alone suffering 12.5 million deaths, almost 60 percent of the total. (U.S. flu deaths, by contrast, constituted only 3 percent of the world total.) But at an international conference on the history of the great pandemic, held at University of Cape Town in September 2001, medical Niall demographers Johnson Juergen and Mueller challenged Jordan's estimates "as almost ludicrously low." Reviewing modern research, they came to the conclusion that "global mortality from the influenza pandemic appears to have been of the order of 50 million." Moreover, the two warned that "even this vast figure may be substantially lower than the real toll, perhaps, as much as 100 percent understated." In other words, it is possible that mortality was actually closer to 100 million or more than 5 percent of the contemporary world population. In their revision, Indian deaths (mainly in the deadly second wave of influenza after September 1918) are reckoned at 18.5 million, although another scholar thinks 20 million is more likely. 14

What explains the extraordinary mortality in India? "Famine and pandemic," observes I. Mills, "formed a set of mutually exacerbating catastrophes." Indeed, these two factors were exquisitely synchronized during the fall of 1918. As Mills explains in one of the few scholarly articles on the Indian experience, the milder first wave of the pandemic arrived in Bombay in June (via the crew of a troop transport) just as the southwestern monsoon was failing throughout much of western and central India; the resulting drought led to soaring grain prices and famine conditions in Bombay, the Deccan, Gujarat, Berar, and, especially, the Central and United Provinces. (Although not mentioned by Mills, grain exports to England and wartime requisitioning practices undoubtedly contributed to price inflation and food shortages as well.) In September, as the famine was worsening, the second—more deadly— wave of influenza arrived, again via Bombay. 15

What followed was the kind of chain reaction (or positive feedback of disasters) that has become so familiar in the history of the modern Third World. "In Bombay Presidency," writes Mills, "the severe second [influenza] wave came at the time of the harvest of the early crop, and sowing of the late crop. With morbidity estimated to be in excess of 50 percent of the population, and with the concentration of severe attacks in the most productive age range, 20–40 [years], the effect on agricultural production was extreme." The area of grain production decreased by one-fifth while staple food prices doubled. The "absolute lack of any public health organization redoubled infection's impact upon the famished population." The Raj heavily taxed the

peasantry to support the Indian Army but spent virtually nothing on rural medicine. ("The Surgeon-General conceded that mortality would have been reduced had it been possible to provide immediate medical aid and suitable nourishment to those attacked.")<sup>17</sup> The American missionary Samuel Higginbottom, who was director of agriculture in the state of Gwalior, wrote to a friend that "influenza has been fearful. Hundreds of bodies daily floating in the river. No official figures have been published for India as a whole, but in villages in Gwalior State that are under my charge the death rate during October and November was from 20 to 60 percent. Cholera, plague, and other epidemics from which India suffers have never shown such a death rate as Influenza."<sup>18</sup>

Desperate refugees from the countryside flooded into the slum districts of Bombay and other cities; there, influenza cut them down by the tens of thousands, "like rats without succour," according to the nationalist paper Young *India.* 19 Mortality, Mills emphasizes, was strictly "class" oriented," with almost eight times as many deaths among low-caste people in Bombay as among Europeans or wealthy Indians—the poor seemed to have been the victims synergy between sinister malnutrition. suppressed their immune response to infection, and rampant bacterial pneumonia. Outside of the crowded urban slums, flu mortality was generally highest in the famished west of India rather than in the east, where the crops had not failed.

Presumably hunger played a similar role in influenza mortality in China, the East Indies, and even Germany, where the Allied blockade had reduced the caloric intake of the urban poor, especially women and children, to dangerous levels. Certainly, every writer on the pandemic has noted its particular affinity for poverty, substandard housing, and inadequate diets. The slum districts of port cities, from Boston to Bombay, seemed to offer especially favorable conditions for spread of the pandemic in its more virulent form.<sup>21</sup>

The pandemic also formed lucrative partnerships with other epidemic diseases. Iran was a grim case in point: according to a careful study by historian Amir Afkhami, the nation of 11 million suffered the greatest relative mortality of any major country, between 8 and 22 percent of the total population. The pandemic hitchhiked the military supply route from Bombay to the British occupation force in this supposedly neutral country. Iran was already reeling from several years of drought, famine, cholera outbreaks, and the depredations of marauding armies. In addition, the callously aggravated had the British famine requisitioning the grain surplus from the large estates, leaving little for a hungry population.<sup>22</sup>

But Akfhami argues that the principal multiplier of influenza mortality in Iran, even more than hunger, was malaria. He finds dramatic correlations between malaria incidence and influenza mortality, both among the local population and the Indian troops of the British Army. Cities with chronic malaria, such as Mashhad, had influenza death rates triple those of cities with low malaria rates, such as Tehran. The climax of pandemic mortality in November coincided with the usual "peak period of malignant tertian"

malarial fevers among Iranians." Akfhami also observes that malaria sufferers, including both Iranians and Indians, were afflicted with anemia and were notoriously susceptible to pulmonary infections. 23

Poverty, malnutrition, chronic illness, and co-infection were thus powerful determinants of the precise tax that the 1918 influenza exacted from different populations. Indeed, the global pandemic itself was really a constellation of individual epidemics, each shaped by local socioeconomic and public-health conditions. In some countries, such as India and Iran, the co-factors (hunger, malaria, anemia) formed deadly nonlinear synergies with influenza and its secondary infections. Although most of the literature on the 1918 pandemic has focused on its unusual preference for young adults, including the robust and well-fed young soldiers of the American Expeditionary Force in France, the correlation between social class and lethality in virtually every country was no less striking.

## CHAPTER 2: BIRDS OF HONG KONG

A new phase seems to have begun in the evolution of avian flu viruses. They have found their way directly to man.<sup>1</sup>

Jaap Goudsmit

In April 1997, Hong Kong issued a set of postage stamps celebrating the migratory birds that flock each winter to the city's Deep Bay and the Mai Po marshes. Deep Bay's mangrove swamps are a freshwater/saltwater interface "rich with pickings for birds," while Mai Po, although now surrounded by the skyscraper New Towns of Yuen Long and Tin Shui Wai, is such a luxuriant bird habitat that it has been designated "a wetland of international importance." In 1997, moreover, the poultry industry was still thriving in the New Territories, supplying ducks, geese, and chickens for sale in the live-poultry markets (also called "wet markets") that are such colorful parts of the urban mosaic.

One of the birds depicted on a new stamp is a handsome, medium-sized duck called a falcated teal. The drakes—somewhat larger than their North American cousins—have dark bills, white throats, and glossy green heads and crests. The teals breed in eastern Siberia before their annual fall migration to the Pearl River Delta and the Mai Po marshes.

They like to forage in rice fields or float in freshwater ponds, where they often come into contact with the domestic ducks that are such an integral part of south Chinese agriculture. Among the flu subtypes identified in a Hong Kong teal is H5N1. That might well make the falcated teal the duck of the apocalypse.

In March 1997, a month before the bird stamps were issued, chickens started dying on a farm near Yuen Long and the Mai Po marshes; they displayed the unmistakable violent symptoms of Highly Pathogenic Avian Influenza (HPAI). As Pete Davies explains in his account of the outbreak: "It's an ugly business. The virus spreads through the bloodstream to infect every tissue and organ; the brain, stomach, lungs, and eyes all leak blood in a body-wide hemorrhage until, from the tips of their combs to the claws on their feet, the birds literally melt." The disease spread to two nearby poultry farms, and as is so often the case with HPAI outbreaks, almost all the birds died. The virus was identified by Hong Kong University researchers as H5N1, a subtype first isolated in 1959.

The gruesome pathology of so-called "fowl plague" was first described in 1878, but the pathogen was not confirmed as influenza A until 1955. Like all influenza, HPAI is essentially mysterious: it flares up unexpectedly among chickens and turkeys in different countries, continents, and hemispheres. Until recently, it has been relatively rare, with fifteen localized outbreaks between 1959 and its sudden appearance in Hong Kong in 1997. HPAI in all of these instances was caused by influenza subtypes containing either H5 or H7; researchers believe that these

hemagglutinins contain extra basic amino acids at their cleavage sites that amplify virulence by allowing viruses to invade a broader variety of tissues and, possibly, species. But there was no evidence at all to suggest that these avian superviruses posed any threat to humans, not even to the poultry workers who tended the ill birds and cleaned up in the aftermath of HPAI's carnage. The species barrier was believed to be insurmountable. 5

After agricultural authorities killed off the remaining sick chickens in April, HPAI seemingly disappeared. Then in mid-May a three-year-old boy—previously in perfect health was admitted to Queen Elizabeth Hospital in Kowloon with a sore throat, fever, and abdominal pain. Despite top-flight intensive care, his condition deteriorated catastrophically, and he died on May 21. Physicians and nurses were appalled by the relentless cascade of disasters that wracked his tiny body: viral pneumonia, acute respiratory distress syndrome (ARDS), Reye's syndrome, and finally, kidney and liver failure. The local department of health ran tests on secretions from the dead child's throat and found an unusual influenza sub-type that it could not identify; frozen samples were sent off in June to two of WHO's four collaborating centers (CDC in Atlanta and NIMR in London), as well as to the National Influenza Center in Rotterdam.

The team in Rotterdam was the first to uncover the lethal strain's identity. Baffled by the failure of the virus to react with any of their antisera, in early August they tested it against a long-shot H5N1 reagent that had been brought back from the Memphis laboratory of the famous influenza

authority Robert Webster. To the consternation of the Rotterdam team, it was a positive match.<sup>6</sup>

The Dutch result was soon confirmed by Atlanta and London, but no one was yet ready to accept that H5N1 had actually vaulted the species barrier and killed the child in Hong Kong. It seemed more plausible that Hong Kong public-health scientists had unwittingly submitted contaminated sample. Leaving nothing to conjecture, the Dutch, followed by the CDC and WHO, sent experts, including Webster, to double-check conditions in the Hong Kong lab. They soon discovered that the Chinese had been scrupulous procedures—there in their contamination. H5N1 was indeed the killer, and as Webster later discovered, it was almost identical to the strain that had killed the chickens in March. A slight hemagglutinin mutation—a difference of only three amino acids—had apparently allowed the bird virus to open the lock on human cells and infect the child. 7

It was a staggering, paradigm-shifting discovery. This H5N1 was not a reassortant, as textbooks predicted, but an avian virus that had come to roost in the human body with a little help from genetic drift. Having made such a seemingly impossible species leap, moreover, there was no theoretical reason why H5N1 could not subsequently reassort with human flu genes in the lungs of a co-infected human; pigs might not be the virus's indispensable intermediaries after all. A pandemic of frightening lethality therefore might be imminent, and it was desperately important for the team of international flu experts in Hong Kong to uncover the exact circumstances of the child's infection.

The most obvious hypothesis—that he had encountered sick chickens at one of the New Territory farms or in a local live-poultry market—turned out to be unlikely. Indeed, the only plausible avian contact that researchers could establish were some chicks and ducklings that had been pets at his preschool; the baby birds had died mysteriously, but when researchers painstakingly tested dust in the playroom they could find no sign of the virus. On the other hand, extensive blood testing revealed that a handful of the child's contacts, including a playmate, a nurse, and a few others (but not his immediate family), had antibodies to H5N1. Five poultry workers also displayed immunological evidence of contact with the virus, but none had become sick. Meanwhile, the trail grew cold, and no more cases appeared: perhaps the child's death had been a fluke. The international experts returned home.

Virologists remained unsettled by the fierce behavior of H5N1/97 in the laboratory. "It reproduced much faster than ordinary flu strains, and in cells that ordinary flu strains couldn't live in, and if you grew it in eggs, it killed them. This virus, said Lim [a Hong Kong scientist], was like an alien." Indeed, when veterinary researchers in Athens, Georgia, infected a poultry flock with the recently isolated human strain, the entire flock died within a day. Horrified scientists, who had never seen such a rapid killer, immediately donned biohazard containment suits and dosed themselves with antivirals; this ignited a controversy about the safety protocols necessary for work with the Hong Kong virus. Influenza diagnostic labs, at least in the United States, were not equipped with the elaborate containment

systems required for working with such a potent virus: biosafety guidelines had not anticipated an influenza that acted like the nightmare protagonist of a scifi thriller. A majority of the research community now decided that H5N1 research should be confined to a small number of Biosafety Level 3-plus or Level 4 labs, but a few scientists chafed under the restrictions (and were later accused of cutting corners on safety). Lurking in the memory of the the background was unexpected resurrection of the H1N1 virus in 1977, an outbreak that almost certainly resulted from the inadvertent escape of the strain from a Russian, or possibly Chinese, laboratory.<sup>8</sup>

None of the journalistic accounts of the 1997 outbreak mention the extreme weather, but it was the wettest year in Hong Kong's meteorological record—a massive Pacific El Niño event brought typhoons and torrential rain to southern China throughout the summer. (Did the deluges wash away the poultry excrement that spread the infection?) The city was still soaked when the pandemic threat suddenly returned at the beginning of winter. A sixwith heart problems was year-old hospitalized November 6 with ordinary flu symptoms; he recovered quickly, but the lab assay confirmed he had H5N1. Two weeks later, a teenager and two adults—all unrelated were hospitalized with the virus. State-of-the-art intensive care failed to prevent the onset of viral pneumonia or other macabre complications like those that had killed the toddler in May; two of the patients died in December. Meanwhile, flu experts from Atlanta, Memphis, and Tokyo were flying

back to Hong Kong. The WHO set up a special Pandemic Task Force and expected the worst.

The city was on the edge of panic. Although Hong Kong had just been returned to Chinese sovereignty, the local press was unfettered in its coverage of the new outbreak. Opposition politicians hammered the administration of Tung Chee-hwa for any perceived hesitancy in its response to the threat. Throughout December public anxiety was reinforced by the seemingly random fashion in which new human cases were appearing across the territory. In addition, the regular flu season had started early, thus increasing the chance of co-infection and reassortment between H5N1 and the prevailing H3N2 human virus.

Parallels with 1918 were becoming obvious. Like its ancestor, H5N1 was now focusing its virulence on healthy adults. Of the seventeen new cases diagnosed between early November and the end of December, eight children, happily, all recovered, with few complications; five of the nine teenage and adult victims, however, were destroyed by viral pneumonia and ARDS. The silver lining (and scientific paradox) was that the virus's success in replicating so efficiently inside humans was not yet matched by equivalent transmissibility. Nonetheless, frantic Hong Kong authorities bought up a large share of the available world supply of the antiviral medication rimantadine as a precaution.

Then in mid-December the "missing link in the epidemiology of avian influenza" suddenly revealed itself: chickens started dropping dead on poultry farms and in the city's markets. The poultry epidemic that had vanished in the spring was now everywhere: H5N1 infected at least 20

percent of the city's chickens, as well as a few domestic ducks and geese. The virus load in the city's birds seemed to be approaching some kind of ominous critical mass, but precedent understanding for there was no consequences of such a large-scale animal epidemic in the heart of a great city. Public-health workers, however, did establish that most of the sick humans had had direct contact with poultry, which made it less likely that H5N1 had succeeded in passing from person to person. $\frac{10}{10}$  On the other hand, some of the infected poultry had come from Guangdong and scientists worried that a stealth epidemic either undiagnosed or concealed for political reasons already existed in other parts of the Pearl River Delta. (Evidence later would emerge of an epidemic among geese in Guangdong the previous year.)

Hong Kong's local government could not make public-health decisions for the rest of China, but it acted decisively to protect its own citizens. Warned by scientists that there was not a second to lose, on December 27 authorities ordered the destruction of all 1.6 million live poultry within the city and its environs; they also embargoed the import of live birds from Guangdong and disinfected the city's markets.

The day before the slaughter, a Filipina domestic worker was diagnosed with bird flu, and the whole city worried whom would be next—every sneeze, cough, and fever that winter was a source of anxiety. Day after day, week after week, health workers nervously tested and retested every case of serious influenza or respiratory distress. Apart from the domestic worker who died in mid-January, they found no

further trace of H5N1, and so the economic crisis in Southeast Asia began to displace flu from the headlines again. Authorities very cautiously allowed the sale of live chickens and other terrestrial poultry to resume, although live ducks and geese were banned; in addition, all poultry imported from Guangdong was now screened for influenza.

celebrated authorities a victory although researchers knew that "an H5N1 pandemic had been averted rather than prevented." A trio of Hong Kong microbiologists who had been at the eye of the storm—Yi Guan, Malik Peiris, and Ken Shortridge—wrote that "the H5N1/97 virus was possibly one or two mutational events from achieving pandemicity." These researchers also began to unravel the virus's genealogy. They found evidence that aquatic bird influenzas had reassorted themselves within the mixing vessel of a quail before jumping to chickens. The two water birds were likely a goose, and yes, possibly a teal. $\frac{11}{}$ 

## CHAPTER 3: A MESSY STORY

An outbreak, like a story, should have a coherent plot. Philip Mortimer

In 1993, Oxford University Press published a collection of essays, edited by Rockefeller University's Stephen Morse, on new and reemergent viruses. Written in the shadow of the AIDS pandemic and the Ebola outbreak in Africa, *Emerging Viruses* warned that global economic and environmental change were speeding the evolution and interspecies transmission of new viruses, some of which might be as deadly as HIV. In his foreword, Richard Krause of the National Institutes of Health pointed to the new ecologies of disease resulting from globalization. "Microbes thrive in these 'undercurrents of opportunity' that arise through social economic change, changes in human behavior, and catastrophic events.... They may fan a minor outbreak into a widespread epidemic."<sup>2</sup>

One such catastrophic event is Third World urbanization, which is shifting the burden of global poverty from the countrysides to the slum peripheries of new megacities. Ninety-five percent of future world population growth will be in the poor cities of the South, with immense consequences for the ecology of disease. This concentration

of the world population in deprived conditions, more than global population growth per se, undergirds what William McNeill calls the "Law of the Conservation of Catastrophe." 3

McNeill is a well known University of Chicago historian of disease ecology. He writes:

It is obvious that as virus host populations (or potential host populations) increase, there is concomitant increase in the probability of major evolutionary changes in virus populations due to increased opportunities for replication, mutation, recombination, and selection. As the world population of humans (and of their domestic animals and plants) increase, the probability for new viral disease outbreaks must inevitably increase as well. AIDS is not the first 'new' virus disease of humans, and it will not be the last. 4

"From the point of view of a hungry virus," McNeill writes in another piece, "we offer a magnificent feeding ground with all our billions of human bodies, where, in the very recent past, there were only half as many people." 5

How is McNeill's gloomy principle actually woven into the complex fabric of a human-influenced biosphere? In one of the rare studies that has actually attempted to conceptualize the vast web of interconnection between urbanization, the world economy, and the natural environment, an international scientific team recently looked at the implications of the soaring bushmeat trade in West Africa. Their 2004 article in *Science* provides an epistemological model for thinking about influenza emergence in south China and elsewhere.

Explosive city growth in West Africa (where the urban population is expected to reach 60 million by 2025) drives an ever-growing demand for animal protein. Traditionally,

West Africans, like many East Asians, have consumed fish as their principal source of protein; fishing, moreover, is a major industry, employing nearly a quarter of the workforce in some countries. But local boats have been unable to compete with the modern, government-subsidized fleets from Europe that now trawl the Gulf of Guinea. These big factory fleets, along with foreign-flag pirate fishers, "illegally extract fish of the highest commercial value, while ... dumping 70 to 90 percent of their haul as by-catch." As a result, fish biomass has fallen by at least half since 1977, and fish have become scarcer and more expensive in local markets. Increasingly bushmeat (the generic name for the species of terrestrial different flesh of some 400 vertebrates) has been substituted for fish—yearly some 400,000 tons of wild game now end up on West African dinner plates. Like the practices that led to declining fish stocks, this level of hunting is unsustainable, and mammal biomass is now decreasing at a rate that fundamentally threatens wildlife diversity.

The authors of this fascinating and troubling study, however, fail to connect a few all-important dots in the causal chain, although undoubtedly they are aware of their importance. One is deforestation, as largely foreign logging companies denude West Africa's remaining coastal rain forests. The bushmeat trade is indissolubly linked to this logging juggernaut and the food needs of its workers, although hunters also poach within official wildlife reserves as well, with the inevitable result being radically increased biological contact between humans and wild animals. The formerly isolated microbiological reservoirs of the rain

forests and mountains have been inadvertently integrated into the food economy of the cities—and the result of this "undercurrent of opportunity" has been a series of viral leaps from animals to humans. The most infamous, of course, is HIV/AIDS: researchers believe that HIV-1 arose as a result of humans eating chimpanzees, while HIV-2 (specific to West Africa) has been linked to the consumption of sooty mangabeys.<sup>7</sup>

There is every reason to believe that the ecological impact of the recent urban-industrial revolution in south China has been just as profound and far-reaching as urban population growth in West Africa. Guangdong—long considered the epicenter of influenza evolution—has become the world's leading export-manufacturing platform, a postmodern Manchester whose toys, running shoes, sports clothing, and cheap electronics are consumed in every corner of the earth. From 1978 until 2002, the province's GDP grew at an astonishing 13.4 percent per year, and the urban population of the Pearl River Delta area increased from 32 percent to 70 percent of the total This spectacular regional transformation, population. crowned by the return of Hong Kong to China in 1997, has accompanied bv a series of socioeconomic been developments that are also likely to reinforce Guangdong's primacy as a viral exporter.

Key parameters of influenza emergence include human and animal population densities, intensity of contact between different species, and the prevalence of chronic respiratory or immune disorders. Population densities are very high in the Delta, with about 1,273 persons per square kilometer. A large segment of the population (indeed, the majority in the industrial boomtown of Shenzhen) are rural immigrants or "floaters" in perpetual motion between city and thousands of rural villages. Without permanent residency permits, these workers live in overcrowded dormitories or slums and are less likely than the registered population to have access to modern medicine. Meanwhile, the state's share of health-care spending has fallen sharply (from 34 percent in 1978 to less than 20 percent in 2003) since the advent of a market economy. "[A]bout 50 percent of people who are sick," explains Yanzhong Huang, "do not see a doctor because of the extremely high out-of-pocket payments." And rampant industrialization has increased exposure to all sorts of environmental hazards and toxins. The Delta, for example, has monstrous air pollution: twenty-four times higher than the rest of China. The population accordingly suffers from all the classical respiratory problems (and, probably, cancers) associated with industrial smog and high sulfur dioxide emissions.

Thanks especially to the prevalence of wet markets in the cities, the urbanization of Guangdong has probably intensified rather than decreased microbial traffic between humans and animals. As income has risen with industrial employment, the population is eating more meat and less rice and vegetables. The most dramatic increase has been in the consumption of poultry, which has more than doubled since 1980. Guangdong is one of China's three largest poultry producers and is home to more than 700 million chickens. An extraordinary concentration of poultry, in

other words, coexists with high human densities, large numbers of pigs, and ubiquitous wild birds. Battery chickens, indeed, "are sometimes kept directly above pig pens, depositing their waste right into the pigs' food troughs." Moreover, as the urban footprint has expanded and farm acreage has contracted, a fractal pattern of garden plots next to dormitories and factories has brought urban population and livestock together in more intimate contact. Finally, Guangdong is also a huge market for wild meat. Unlike West Africa, where subsistence demand drives the bushmeat trade, the Chinese predilection for exotic animals stems from ancient homeopathic beliefs; the demand is inexorable, and Laos (via Vietnam) has become a major supplier of live game. 10

From the beginning of the second wave of H5N1 in the fall of 1997, everyone in Hong Kong was looking nervously over their shoulders at Guangdong and the rest of south China. A newspaper in Beijing reported that there were cases of bird flu in Guangdong but then was forced to retract the story. At the WHO's urging, the CDC sent H5N1 diagnostic kits to researchers in Guangzhou (Canton) and Shenzhen to ensure that everyone doing lab work was using the same protocols. In mid-January, after a brief scuffle over visas, a top-level WHO team was allowed to visit Guangdong for a week.

The WHO visit bore fruit with the adoption in March of an influenza surveillance plan for south China under the administration of the Chinese National Influenza Center; health workers were asked to be particularly vigilant in reporting and monitoring cases of acute respiratory disease. No human cases of H5N1 were found, but Guangdong and the rest of the south were unexpectedly hit by a severe summer epidemic of normal flu: H3N2.

In a simpler universe, as in some microbiology textbooks, each subtype would patiently await its turn at the helm. But in the late winter of 1999, the new surveillance system revealed a claim-jumper: Hong Kong scientists were stunned to discover H9N2 in two children in March, with five "officially unconfirmed" cases simultaneously reported from Guangdong. Although none of the cases were lifethreatening, the discovery of another hole in the species barrier was unnerving. The new strain was very close to an H9N2 isolated from quail the year before by Guan, Peiris, and Shortridge. But it was not the only H9 in town. Surveillance of pigs in a Hong Kong slaughterhouse found animals with the quail strain as well as some with a distinctive H9N2 derived from ducks. Genetic analysis then implicated the H9 quail strain in the viral *ménage* à trois that had generated the 1997 killer. The internal proteins in H5N1 were virtually identical with those from H9N2. 12

With this double recognition that H9N2 was a precursor of H5N1 reassortment, as well as a human invader in its own right, the story was getting surprisingly messy. Nonlinear complexity now governed the plot. To gain a better understanding of what was actually happening, the University of Hong Kong research team headed by Guan, Peiris, and Shortridge decided to explore the viral underworld of Guangdong in unprecedented detail. They wanted to find out how many subtypes and strains were circulating in the avian population and, most importantly,

how they were interacting with one another. For a year, starting in July 2000, researchers carefully isolated viruses from ducks in the live-poultry markets of the Guangdong city of Shantou. The results of their study, published in the summer of 2003, fundamentally revised the standard picture of influenza evolution.

of all, they discovered extraordinary unexpected genetic diversity: almost 500 distinct strains of influenza, including fifty-three different iterations of the H9 subtype. Second, they established that reassortment was a more common event than previously imagined. Gene segments were vigorously being traded throughout the diverse network of influenzas. Previously, "influenza gene flow was usually considered to occur from aquatic birds to other animals." Now they found ample evidence that viruses were evolving from ducks to poultry and back again. "The species barriers between the birds have become much more permeable than previously anticipated. Increasing the heterogeneity of influenza viruses in these hosts results in an enlarged and dynamic influenza gene pool in continuous flux rather than one that is limited to aquatic birds and therefore in evolutionary stasis." Or, as American virologist Richard Webby pithily put it, "we have a bucket of evolution going on."14

The industrialization of south China, perhaps, had altered crucial parameters in an already very complex ecological system, exponentially expanding the surface area of contact between avian and nonavian influenzas. As the rate of interspecies transmission of influenza accelerated, so too did the evolution of protopandemic strains. The Hong

Kong research team had discovered, in other words, that contemporary influenza, like a postmodern novel, has no single narrative, but rather disparate storylines racing one another to dictate a bloody conclusion.

Meanwhile, H5N1 was again laying siege to Hong Kong. Between February and March 2001, the surveillance network found several strains of the virus among market chickens, quail, pheasants, and pigeons. A few months later, South Korean authorities isolated H5N1 in imported Chinese duck meat. Laboratory testing subsequently revealed that these H5N1 genotypes were a separate reassortment from the 1997 strain and had most likely originated sometime in late 2000 from goose viruses that had "crossed to ducks and re-assorted with other unknown influenza viruses of aquatic origin." Researchers were horrified to discover that the new H5N1 was even more pathogenic than the old. In May chickens started dying again in the city's markets, and once more the city government mandated a slaughter of local poultry before the new strains infected humans or reassorted with  $H9N2.\frac{15}{}$ 

With so much heavy genetic traffic between feral avian reservoirs, domestic poultry, and mammals, researchers were becoming pessimistic about the likelihood of successfully containing further outbreaks by local culling of birds. When H5N1 returned again in February 2002, top virologist Yi Guan of the University of Hong Kong told *China Daily* that truly drastic action was now necessary— live poultry had to go. Guan said, "I believe that we have to get rid of the farms, and the poultry markets, and the import of

fresh chickens." The poultry industry—seemingly oblivious to the nature of the pandemic threat— screamed that the scientists had gone berserk. "Avian influenza is just like any human flu—you just cannot get rid of it. However, it does not make sense to get rid of the poultry industry to get rid of the bird flu. That would be an ignorant act." The authorities seemingly agreed, and they restricted their response to ordering the destruction of another 900,000 chickens.

In December, textbook theory was again confounded as H5N1 began to decimate its natural hosts. Ducks, as well as geese, flamingos, swans, egrets, and herons, started dying in two popular Hong Kong parks; mallards—presumed immune to the pathogenic effects of influenza—developed catastrophic neurological disorders. The dead ducks were incontrovertible proof that a two-way flow of H5N1 mutants now existed between aquatic and terrestrial birds. 17 Scientists worried that antigenic drift had been accelerated by the illegal use of unregistered poultry vaccines in Guangdong. Other researchers speculated that lethal strains of H5N1 might spread through the wild duck population and follow the annual migration back to Siberian or even Alaskan lakes. 18 (In 2004, the United Nations' Food and Agriculture Organization [FAO] learned that Russian researchers in Novosibirsk had indeed found H5N1—95 percent similar to the Hong Kong strain—the previous year in a wild mallard duck on Lake Chany in western Siberia.)<sup>19</sup> In any event, as Shortridge, Peiris, and Guan glumly pointed out in an article, it was now evident that the H5N1 had become "non-eradicable." 20 infection in birds

Meanwhile, Hong Kong closed its parks and slaughtered its beloved wild birds.

Two months later, at the beginning of February 2003, a seven-year-old girl died of an acute respiratory disease while visiting a Fujian province in the company of her mother, sister, and brother. She was buried before the exact cause of death could be ascertained. Her father, who rushed from Hong Kong to his dying daughter's bedside, was also stricken and died in mid-February, nine days after his return to Hong Kong; his eight-year-old son developed critical symptoms of respiratory distress but ultimately recovered. 21 Both father and son were confirmed to have been infected with the same strain of H5N1 that was killing ducks in the parks. Genetic sequencing revealed that it was remote cousin to the original 1997 strain. hemagglutinin was derived from the same lineage, but the proteins and neuraminidase had internal evolved elsewhere. Some researchers surmised that the influenza had been contracted in Fujian—the family's relatives kept chickens—and were skeptical of China's claim that it had experienced any large-scale outbreaks of avian influenza among ducks or poultry.<sup>22</sup> In any event, experts were troubled by further evidence of increasing virulence in the rapidly evolving H5N1 family. WHO went to pandemic alert status, and public-health officials again buckled their seat belts.

## CHAPTER 4: PANDEMIC SURPRISE

Humankind has had a lucky escape. 1

Robin Weiss and Angela McLean

Shortly before the isolation of the new avian-to-human H5N1 in Hong Kong in 2003, the WHO office in Beijing received an email warning that a "strange contagious disease" had killed more than one hundred people in Guangdong in a single week. Medical workers and foodhandlers were said to be especially affected. In the capital of Guangzhou (Canton), provincial panicked residents were buying up surgical masks and antibiotics as well as white vinegar, a traditional folk treatment for respiratory illness. Over the next few days, Chinese publichealth officials grudgingly acknowledged that five people had died from "atypical pneumonia"; the outbreak had started in Foshan the previous November, had infected about 300 people, but was now "under control." The Chinese were admitting, in effect, that they had concealed the epidemic from the WHO, but were now urging the world "not to worry"—they emphasized that the victims had all tested negative for influenza. But provincial and national authorities gave conflicting accounts of the likely pathogen: blamed Guangdong bacterium *Mycoplasma* the

pneumoniae, while Beijing insisted that it was actually Chlamydia. To further erode credibility, "a spokesman for the Guangdong health department told reporters that all further information would be disseminated by the party propaganda unit." Although these prohibitions did not stop the Internet from gushing rumors, authorities also threatened that "any physician or journalist who reported on the disease would risk being persecuted for leaking state secrets." Secrets."

Veteran influenza researchers were highly skeptical of the official Chinese account. With avian influenza again killing birds in Hong Kong, it was logical to suspect that the mysterious pneumonia was, in fact, the beginning of the long-dreaded pandemic. The reports from Guangdong, moreover, were soon followed by the identification of the two, possibly three, human H5N1 cases: Could this be just a coincidence? Circumstantial evidence supported the worst-case scenario. It also followed that if the disease were in Hong Kong, south China's portal to the world, the virus might escape on the first available plane.

As investigators later reconstructed the itinerary, this is exactly what happened in the third week of February. A doctor from Guangzhou who had been attending victims of the pneumonia, arrived in Hong Kong on February 21 for a family wedding. Already ill, he checked into a room on the ninth floor of the Metropole Hotel, where by some unidentified mechanism, he managed to transmit his virus to sixteen other guests on the same floor—in the parlance of epidemiology, the doctor was a "superspreader." The CDC would later construct a flowchart of cases that

originated from the Metropole Hotel: 195 in Hong Kong, 71 in Singapore, 58 in Vietnam, 29 in Canada, and 1 each in Ireland and the United States. As WHO Global Outbreak Alert and Response scientists later marveled, "A global outbreak was thus seeded from a single person on a single day on a single floor of a Hong Kong hotel."<sup>4</sup>

The first Metropole case to attract WHO attention was a Chinese American businessman who became desperately ill in Hanoi. Local hospital staff, petrified by the possibility that it was a case of avian flu, asked the local WHO representative, Dr. Carlo Urbani, to oversee the patient. The Italian doctor alerted the WHO Regional Office for the Western Pacific on February 28 that the mystery disease was now a traveler, and there were soon outbreaks in several other countries. On March 1, with several patients already hospitalized in Hong Kong, a female flight attendant (the first of several Metropole victims) was admitted to a Singapore hospital with acute respiratory distress. A few days later, an elderly Canadian who had stayed in the Metropole died in Toronto, and five members of her family were soon hospitalized. Meanwhile, in a pattern that confirmed rumors from Guangdong, hospital workers who had been exposed to the Metropole patients in Hong Kong and Hanoi developed symptoms; the French Hospital in Hanoi was forced to close. Next, the Chinese American businessman died, followed by the son of the elderly Toronto woman. By mid-March, scores of medical personnel in Hanoi and Hong Kong were in intensive care, and Ontario officials had to seal off Scarborough Grace Hospital. Dr. Urbani developed the disease and was evacuated from Hanoi to a hospital in Thailand, where he died on March 29. By this time, some frightened hospital staff in China, Canada, and Vietnam refused to treat patients diagnosed with the enigmatic, deadly illness.

it avian influenza? The pathogen was still unidentified on March 15 when the WHO labeled the disease after its symptoms: Severe Acute Respiratory Syndrome, or SARS. On that same day, a Singaporean physician, returning medical from a conference in New York, was hospitalized during a stopover in Frankfurt along with his pregnant wife and mother-inlaw. The doctor had treated the stewardess in Singapore: another superspreader, she would ultimately be the source of almost one hundred other cases. Although WHO finally issued a warning to the airline industry, it came too late to prevent other infected passengers from subsequently carrying SARS to Beijing and Taiwan. At the end of March, both Hong Kong and Toronto authorities were pressed to take more drastic action. Hong Kong officials closed schools and put more than 1,080 residents under quarantine, while in Toronto, another hospital was closed off and thousands of hospital workers and others in contact with SARS cases were asked to quarantine themselves at home.

In Hong Kong, the epidemic assumed nightmarish proportions in the Amoy Gardens housing complex in Kowloon. Tower Block E was thirty-three stories high with eight apartments on each floor; the virus was first brought to the building in mid-March by a resident's brother, who had recently undergone dialysis at the SARS-infected Prince of Wales Hospital. He was suffering badly from

diarrhea and used his brother's toilet. Within a few days, an extraordinary 321 residents of Block E and adjoining buildings developed SARS. The mode of transmission remains a mystery. Although some experts insist that the contagion had to be airborne (perhaps as residents shared elevators), Department of Health officials concluded that SARS was disseminated, at least in part, through faulty plumbing that brought residents "into contact with small droplets containing viruses from the contaminated sewage." The Amoy Gardens incident was particularly troubling because it demonstrated that in conditions of extreme urban density—such as those found in high-rise housing, hospitals, and slums—viral transmission might be potently amplified by faulty ventilation and sewage systems, or, worse, by those systems' absence.<sup>5</sup>

Meanwhile. SARS had become a test of China's international credibility, with Health Minister Wenkang continuing to antagonize the world public-health community with his perfunctory and reliably inaccurate reports on the epidemic. Since early February, WHO experts had urgently wanted to visit Guangdong to investigate conditions there, but the Health Ministry obstructed the mission until the beginning of April—by then, SARS has set Beijing ablaze as well. China's "official secrets" law had prevented Guangdong officials from briefing other local health authorities about the disease, so when the first cases appeared in Beijing in early March, local doctors were clueless. When the WHO team flew to Beijing, they were initially blocked from inspecting the military hospitals where most of the victims were being

treated. Although officials continued to assert that the epidemic was contained, on April 16 the WHO took the unprecedented step of chastising the Chinese government for "inadequate reporting" of SARS cases.<sup>6</sup>

Chinese leaders were deeply worried about the impact of the epidemic upon trade and economic growth. SARS, says Yanzhong Huang in a fascinating account, "caused the most severe sociopolitical crisis for the Chinese leadership since the 1989 Tiananmen crackdown." China's stillpowerful former president, Jiang Zemin, reputedly urged strict censorship, while his successor, Hu Jintao, favored disclosure and collaboration with the WHO. Old-quard Beijing officials tried to conceal the full extent of the new epidemic not only from the outside world but even from high-ranking officials in the Zemin faction. When the WHO, for the first time in its history, advised visitors to stay away from Hong Kong and Guangdong, the health minister responded that SARS had been contained and that south China was completely safe for visitors. A courageous whistleblower, a retired military surgeon named Jiang Yanyong, who had treated many victims of the Tiananmen Square massacre, circulated an email that accused the minister of bald-faced lying. *Time* magazine covered the story and, according to Huang, "triggered a political earthquake in Beijing."<sup>7</sup>

President Hu Jintao and his supporters now took firm command of the situation: bureaucratic duplicity and inaction were replaced by an almost Maoist display of partystate willpower. The equivalent of 1 billion dollars in state aid (a fraction of the economic damage already caused to

China and Hong Kong) was made available to upgrade local hospitals and public-health services. Health Minister Zhang Wenkang and Beijing mayor Meng Xuenong—both Zemin loyalists—were purged, and other officials were bluntly told that their survival depended upon extirpating SARS. "Driven by political zeal, they sealed off villages, apartment complexes, and university campuses, quarantined tens of thousands of people, and set up checkpoints to take temperatures.... In Guangdong, 80 million people were mobilized to clean houses and streets. In the countryside, virtually every village was on SARS alert, with roadside booths installed to examine all those who entered or left." To the surprise of many, these draconian quarantines -"momentous measures," says Yanzhong Huang-seemed to work. The spread of the SARS epidemic inside China was arrested, and in late June the WHO canceled its warnings about travel to Hong Kong and Beijing.<sup>8</sup>

While the drama inside China was unfolding, a WHO-organized virtual consortium of laboratories was working night and day to discover the cause of SARS. Within a month, this unprecedented research effort, spearheaded by Malik Peiris and his colleagues in Hong Kong and Shenzhen, had isolated a coronavirus. Although scientists were greatly relieved that it was not "the Big One" (an influenza pandemic) after all, they were flabbergasted that a member of a viral family normally associated with mild colds and diarrhea had become an international serial killer. And as researchers sequenced the genome of the SARS virus, they found little link to any of the known

human-adapted members of the family. The SARS virus was genetically *sui generis*.

There was much speculation about an exotic animal source. Once again, the crack Hong Kong team led by Guan, Peiris, and Shortridge returned to the wet markets, this time in Shenzhen, the boomtown neighbor of Hong Kong. Among caged animals in the retail wildlife market, they soon found the SARS virus in a group of masked palm civets and a raccoon dog; a Chinese ferret badger also showed evidence of SARS antibodies. All three small carnivores are considered luxury or health items in the diet of Guangdong urban dwellers. (Ironically, civets are eaten because of a homeopathic belief that they provide immunity influenza.) They are also lucrative commodities in the booming south China bushmeat trade that includes imports from Laos and Vietnam. SARS, then, like HIV, was a deadly by-product of a largely illegal international wild-life trade, intimately connected with logging and deforestation, which mortally threatens human health as well as regional biodiversity. 10

The WHO officially declared the SARS outbreaks contained on July 5. (A small-scale outbreak at the end of 2003, quickly controlled by Chinese authorities, reminded the world that SARS will be a recurrent danger until the prototype vaccine, now being field-tested, becomes widely available.) The first pandemic of the twenty-first century had generated approximately 8,500 cases in 26 countries; nearly 11 percent of SARS patients (916) died worldwide, although mortality in some localities was closer to 20 percent. Like influenza, SARS had a very strong preference

for the elderly, whose death rate was over 50 percent. Young adults, in contrast, had only a 7 percent chance of dying, while SARS was seldom life-threatening to children. 11

The management of the epidemic in Hong Kong and Toronto—each with an identical death rate of 17 percent was the subject of investigation by expert panels in both cities. A summary of their respective findings was published in 2004 by the Journal of the American Medical Association (JAMA). As the panel chairs emphasize: "Both areas were hampered by underinvestment in public-health infrastructure, diminution of public-health leadership, and weak links between health care and public health." In both cities, moreover, the health systems were overwhelmed by the epidemic. No one had expected a disease that targeted hospitals or took such a heavy toll on primary health-care personnel: 22 percent of SARS cases in Hong Kong, 43 percent in Toronto. Early in the Guangdong outbreak, some 90 percent of cases were among health-care workers. The had to import, Ontario government more clandestinely, several hundred U.S. doctors to make up the shortfall caused by ill or frightened physicians. In Hong Kong the hospital system almost broke down because of the lack of infection control in emergency rooms and the shortage of isolation units (single, negative-pressure rooms). In any event, JAMA reported, "neither jurisdiction had enough infection control practitioners and infectious disease specialists." The distressing spread of SARS among medical personnel, however, was not due to the virus's super-infectivity, but, rather, to surprisingly widespread

failure of hospital staff to adhere to proper protective clothing and standard hygiene (such as simple handwashing). In both cities, lines of authority were blurred or contradictory, and general practitioners were often left totally in the dark about diagnostic and therapeutic procedures. In the end, the nineteenth century, not the twenty-first, defeated SARS: "containment of SARS relied heavily on application of public health and clinical infection-control measures rooted in nineteenth-century science." 12

The laboratory manipulation of SARS also revealed dangerous flaws in the biosecurity of many research institutes and universities working with respiratory viruses. In separate incidents in Singapore and Taiwan, researchers managed to infect themselves with SARS. Robert Webster cited these cases in a January 2004 *Lancet* article in which he warned that an influenza pandemic might start with the escape of a dangerous fossil virus such as H2N2, the 1957 pandemic strain against which no one born since 1968 has any immunity. He reminded readers that the sudden reappearance of H1N1 in 1977, after a twenty-year hiatus, was probably the result of a lab accident in Russia or China. 13

The SARS outbreak has also been studied as a real-life test of the preparedness of world organizations, national governments, and local health systems to respond to an influenza pandemic. "The quick and effective response of the WHO to SARS," reported British experts to the Royal Society, "did much to restore faith among the many critics of the effectiveness of international agencies with large bureaucracies and limited resources for action." But they

warned that the successful containment of the SARS pandemic had sowed the illusion that the "system works," when, in their view, the system was simply "very lucky." The "simple public health measures that worked well for SARS" are "unlikely to be effective" in the case of an "antigentically novel influenza virus, of both high pathogenicity and transmissibility." "Sentiments of the type 'we have been successful once—we will be again' may be far from the truth." 14

What are the key differences between SARS and influenza? Although SARS produces similar symptoms, it is not nearly as "subtle" as influenza. 15 As Peiris and Guan emphasize, "SARS manifested several features that made it more amenable to control through public health measures than some other potential emerging infectious disease threats." 16 In the first place, SARS needs about five days to incubate and does not usually become contagious until well after the onset of fever and dry coughing; infectiousness takes about ten days to peak, and research has found few asymptomatic infections without sickness. The old-fashioned quarantine, if ruthlessly tactics of isolation and implemented, can work effectively against such a slowdeveloping virus whose symptoms consistently signal infectiousness.

Influenza is an altogether different story. It is fast and deceptive, and infectiousness and sickness do not coincide; an infected person massively sheds virus and becomes highly contagious a day or more before the actual onset of symptoms. (HIV, with its long, silent incubation period is, of course, even more insidious because the infected person

can be contagious for years without manifesting any symptoms or sickness.) Moreover, influenza epidemics include large numbers of asymptomatic infections: spreaders without symptoms. Influenza, as a result, is more transmissible. In addition, technically it has a higher "R," or "basic reproduction number" (defined as the "average number of secondary cases generated by one primary case in a susceptible population") than does SARS, or for that matter, HIV. A typical flu has an R of 5 to 25, while SARS is only 2 to 3 (not counting the still poorly understood phenomenon of so-called "superspreaders"). To stop an epidemic of SARS, public-health officials need only block viral transmission, either by isolation or quarantine, in about half the cases. Control of pandemic flu, on the other hand, requires an almost 100 percent containment of infection. 17 Traditional isolation measures, accordingly, may not be much more effective tomorrow than they were in 1918.

Finally, the 2002-3 SARS pandemic had a fortuitous geography. China and Singapore were both authoritarian states with the capacity to impose effective, militarized quarantines. (In Singapore this took the Orwellian form of temperature-detecting sensors in the airport and home video-surveillance of hundreds of quarantined individuals.) Guangdong, moreover, by Chinese standards is a rich region with a much more modern health-care infrastructure than poorer inland provinces. Although SARS exposed the Achilles' heel of neglect and underinvestment in their public-health systems, Toronto and Hong Kong are likewise affluent cities with superb laboratory medicine.

SARS in Bangladesh, Afghanistan, or Zaire would have been a different pandemic. This is exactly the "What if?" that haunted the Royal Society's postmortem on the SARS pandemic: "[S]uppose the virus had flown from Hong Kong to Durban instead of Toronto. It is a city of similar size but without a similar health infrastructure, and with a significant proportion inhabitants of its immunecompromised owing to HIV-1 infection. Then Africa could have become endemic for SARS by now." 18 An influenza pandemic, to be sure, would not neglect the poor countries of the world.

## CHAPTER 5: THE TRIANGLE OF DOOM

We need to look in our own backyard for where the next pandemic may appear. 1

Christopher Olsen

The SARS pandemic ratified Guangdong's exceptional importance as a disease epicenter. But does Guangdong have a unique franchise? Some influenza experts believe that all pandemics originate in the mixed swine-and-poultry agriculture of south China, a near-dogma that makes them resist compelling evidence that the 1918 reassortant first emerged in Kansas.<sup>2</sup> Other researchers, however, argue that the environmental preconditions rapid for the interspecies evolution of influenza found are now elsewhere, and they point specifically to the ecological impacts of the export-led industrialization of poultry and pork production since the 1980s.

This so-called "Livestock Revolution" has been primarily driven by Third World urbanization and the rising demand in developing countries—above all, China—for poultry, pork, and dairy products. Although Third World urban dwellers are obviously poorer than their OECD counterparts, a much larger percentage of income growth is expended on animal protein, and this is the demand engine that currently drives

huge increases in chicken and swine populations. According to Australian researchers, "The [global] share of meat and milk consumed in developing countries rose from 37 to 53 percent and from 34 to 44 percent, respectively, from 1983 to 1997.... By contrast, both per capita and aggregate milk and meat consumption stagnated in the developed world, where saturation levels of consumption have been reached and population growth is small." From the standpoint of influenza ecology, moreover, it is striking that pork and poultry constitute 76 percent of the developing world's increased meat consumption, and poultry has accounted for almost all of the small net increase in rich countries' food consumption. The viral "food supply"—poultry, swine, and humans— has been dramatically enlarged.

Like the Green Revolution before it, the Livestock Revolution has favored corporate producers rather than peasants and family farmers. As a recent UN report emphasizes, "large-scale, industrial production accounts already for roughly 80 percent of the total production increase in livestock products in Asia since 1990. In the future, most production, especially of pigs and poultry, is expected not to come from traditional production systems that have characterized the region for centuries, but from industrial, large-scale production."4

The world icon of industrialized poultry and livestock production is giant Tyson Foods, which, like Wal-Mart, grew up in hardscrabble Arkansas. Tyson, which kills 2.2 billion chickens annually, has become globally synonymous with scaled-up, vertically coordinated production; exploitation of contract growers; visceral antiunionism; rampant industrial

injury; downstream environmental dumping; and political corruption. The global dominance of behemoths like Tyson has forced local farmers to either integrate with large-scale chicken- and pork-processing firms or perish. "These firms," write Donald Stull and Michael Broadway, "owned not only the broilers they supplied to contract growers, but the eggs that hatched the birds, the feed that went into them, and the plants that processed and then sold them to grocery stores." Whether in the Ozarks, Holland, or Thailand, entire farming districts have been converted to the warehousing of poultry, with farmers serving as little more than chicken custodians. At the same time, livestock has been disintegrated from agriculture; thus creating a new geography where grain and feed production is spatially separate from the raising of chickens and pigs. 6

has been extraordinary population The result concentrations of poultry. A crucial requirement of the modern chicken industry, for example, is "production density," the compact location of broiler farms around a large processing plant. As a result, there are now regions in North America, Brazil, western Europe, and South Asia with chicken populations in the hundreds of millions—in western Arkansas and northern Georgia, for example, more than 1 billion chickens are slaughtered annually. Similarly, the raising of swine is increasingly centralized in huge operations, often adjacent to poultry farms and migratory superurbanization habitats. The of the population, in other words, has been paralleled by an equally dense urbanization of its meat supply. Might not one of these artificial Guangdongs be a pandemic crucible as

well? Could production density become a synonym for viral density?

The answer to these questions was revealed in March 2003. While scientists were desperately trying to figure out the identity of an atypical pneumonia in China, chickens were dying on a farm in the Gelder Valley (Gelderland) of Holland. The Netherlands is the world's leading exporter of eggs and live chickens, as well as a major producer of turkeys and geese; the hundreds of chicken farms in the Gelderland are at the center of the highly rationalized, \$2 billion-per-year Dutch poultry industry. Many of the farms also keep pet flocks of ducks and swans.<sup>8</sup> With its intimate juxtaposition of wetlands, wild birds, poultry, and high urban density, as well as its hub-like role in the European Union's global commerce, the Netherlands recapitulates many of the distinctive features of the Pearl River Delta; the March epidemic, in fact, was later traced back to a farm whose free-range chickens were in contact with wild waterfowl in an adjacent canal.

Although vigilant Dutch agricultural authorities quickly quarantined the movement of chickens and temporarily halted poultry exports, the Highly Pathogenic Avian Influenza (HPAI) swept like wildfire through the Gelderland. The virus was identified as an H7N7 strain more or less identical to a strain isolated in mallards several years earlier. By April, turkeys were dying in North Brabant, and the first HPAI cases were reported in Meeuwen-Gruitrode in neighboring Belgium. Even more disturbingly, evidence of the infection was discovered in pigs on several farms in the Gelderland, increasing the dangerous likelihood of

H7N7's reassortment with swine and human influenzas. (The pigs were promptly slaughtered.) As European Union agricultural experts fretted over the potential for a pan-European epidemic, the Dutch government came under immense domestic and foreign pressure to act more aggressively. The Hague decided to exterminate all the poultry in the Gelderland and other infected areas and to dispose of thousands of tons of virus-laden chicken manure. As thousands of unhappy farmers clamored in protest, crews of poultry workers, aided by the Dutch army, began the epic slaughter of more than 30 million chickens, almost one-third of Holland's entire poultry population. 10

Although HPAI was an enormous threat to the poultry industry, there was little apprehension of any public-health danger. A few years earlier, there had been a serious H7N7 outbreak among chickens in Italy, but sero-logical analysis found no evidence of any transmission to humans. Moreover, all the personnel involved in the Dutch cull wore protective clothing, including goggles and mouth-and-nose masks. Even when a veterinarian who been involved in the early identification of the outbreak developed acute conjunctivitis, experts expressed surprise but not alarm: in 1996. an English duck owner had developed conjunctivitis after contact with a sick bird, and there was an extraordinary case where an avian H7 had been transmitted to a human from a sick seal but did not cause serious illness; H7N7 was also known to be endemic in horses. The virus's modest talent for crossing species barriers had never been accompanied by corresponding virulence—on rare occasions the virus apparently could

inflame cells around the eye but it had shown no ability to replicate in the human respiratory tract or other tissues. $\frac{11}{1}$ 

This benign view of H7N7, however, was quickly challenged by a chorus of complaints from poultry workers with conjunctivitis, and in a few cases, reports of classical flu symptoms. Because some immigrant workers, now unemployed after the cull, had already returned to their native countries, there was concern that they might seed new outbreaks. The prestigious Dutch National Institute of Public Health and the Environment quickly dispatched an expert investigation team, under the leadership of Dr. Marion Koopmans, to the Gelderland. A medical command center was established, and from March 8 nurses visited every household that might have had contact with infected birds. Since the ordinary flu season was in progress, vaccinations were made obligatory for poultry workers and their families, although this policy was implemented too late to prevent several worrisome cases of co-infection by H7N7 and normal H3N1. Meanwhile, the outbreak team was stunned by the scale of infection they discovered: 553 people out of an exposed population of approximately 4,500 reported conjunctivitis or other symptoms; subsequent serological studies demonstrated that, in fact, as many as 2,000 of the exposed group had been infected but not always sickened. Surgical masks and goggles, for whatever reason, had afforded the poultry cullers little or no protection against the virus. 12

Moreover, relatives and housemates of poultry workers, who had no direct contact with infected birds, also developed conjunctivitis. Public-health officials were convinced that the virus had acquired a limited but real ability to spread via person-to-person contact, although the exact mode of transmission was unclear. The outbreak team also found evidence that H7N7 was accumulating dangerous mutations as it passed through the human population. The event's most frightening moment was the death of a fifty-seven-year-old veterinarian on April 19; soon after exposure to sick chickens, he had developed viral pneumonia (and later ARDS) instead of relatively benign conjunctivitis. Previously in good health, he was not immune-compromised, nor did he have any underlying disease. Alarmingly, his catastrophic decline matched the gruesome clinical descriptions of the 1997 deaths in Hong Kong, or for that matter, the acute cases in 1918. 13

An urgent analysis of viral samples removed from the vet's lungs revealed that the strain that killed him was not an avian-human reassortant, as some had feared, but a variant of the original H7N7 virus that had undergone twelve amino acid substitutions. While HA has always been influenza's celebrity protein because of its crucial role in determining host range, and possibly, virulence, the Dutch researchers, like colleagues elsewhere, were coming around to the idea that mutations in internal proteins—such as PB2 or the nonstructural protein NS2—might be important co-factors in the severity of infection. In any event, the Dutch outbreak, with its deadly index case, now had the WHO's attention, even if the world press was diverted by the ongoing battle against SARS. 14

After H7N7's brief forays into Belgium and Germany, the outbreak was officially contained in August. Dutch experts

regarded it as another harrowingly close call with a potentially deadly pandemic. Like the earlier H9 outbreak, the Gelderland epidemic demonstrated that multiple subtypes (including H9, H7, and possibly H4 and H6, as well as reborn H2) were racing H5 to the pandemic finish line. The rapidity and scale of the Dutch outbreak also proved that south China no longer had a monopoly on deadly influenza: there were now multiple epicenters.

The H7N7 crisis also provided an additional reason for public-health officials and human influenza researchers to talk to their expert animal-virus counterparts. In the past, human and veterinary medicines had been parallel sciences that only occasionally intersected during rare interspecies disease events, but now the two viral universes, animal and human, seem to be locked together in a frenetic evolutionary embrace that makes the old dualism seem obsolete. To avoid a catastrophic pandemic surprise, it is urgent to know what is happening on farms months, even years, ahead of any human transmission.

Several specific developments in the wake of the global Livestock Revolution have especially put scientists' nerves on edge. One is the sudden viral chaos on pig farms since 1997. For the previous sixty or seventy years, swine influenza—a lineage derived from the H1N1 of 1918—exhibited extraordinary genetic stability. Although individual pigs occasionally became mixing vessels for avian strains (as many believed happened in 1957 and again in 1968), the H1N1 dynasty was otherwise as unremitting as the Habsburgs. Then in 1997, the hogs on one of North Carolina's megafarms caught H3N2, a human flu; this sub-

type soon reassorted with avian and classic swine viruses, and "by late 1999, the novel viruses could be found wherever there were pigs in North America and so were presumably spread by cross-country transport." 16

The new swine flu pandemic threat apparently has arisen directly from the increasing scale of hog production; researchers told *Science* that swine influenza's sudden burst of mutational energy has probably been stimulated by parallel changes in herd size, interstate transport of hogs, and vaccination practice. Since 1993, U.S. pork production has been restructured around the Tyson, or "poultry model," of very large, industrialized units. In a single decade, from 1993 to 2003, the percentage of hogs raised on factory farms with more than 5,000 animals increased from 18 percent to 53 percent. 17

Increased shipping of hogs over distance simultaneously expands the radius of potential infection. Meanwhile, "in less than a decade, vaccination has become the norm for breeding sows, which in turn pass their maternal antibodies on to their progeny ... but the vaccine is not protecting against all new strains." What seems to be happening, instead, is that influenza vaccinations— like the notorious antibiotics given to steers—are probably selecting for resistant new viral types. In the absence of any official surveillance system for swine flu, a dangerous reassortant could emerge with little warning. 18

Another "in our own backyard" trend that raises anxiety is the prevalence of so-called "Low Pathogenic Avian Influenza" (LPAI); LPAI infections, according to the *Terrestrial Animal Health Code* published by the Office

International des Epizooties (OIE), are endemic in wild birds, causing mild symptoms and low mortality in poultry. In the United States, the Department of Agriculture responds to all HPAI outbreaks, but control of LPAI is left to individual states whose agricultural agencies are often captives of local agribusiness. In an era of crumbling species barriers and increasing pandemic risk, such special-interest federalism poses unacceptable public-health risks: consider the secret LPAI epidemic in California in 2000–2004.

In 2000, an H6N2 influenza began circulating in Southern California poultry. The virus intrigued the scientists who sequenced its genome, because its proteins appeared to derive from both North American and Eurasian lineages of waterfowl.  $\frac{19}{19}$  In its early stages the new virus caused very few clinical symptoms, but it quickly evolved more lethal genotypes. By January 2002 a particularly virulent strain appeared on a San Diego farm and spread to other local poultry ranches; infected hens from Southern California were then shipped to Turlock in the Central Valley. A major poultry processing center, Turlock became the hub of an explosive epidemic. As a study published by the Institute of Medicine explains: "That is when the Turlock region, which is bound by three major roads, became known as the Triangle of Doom: a bird couldn't enter the region without becoming infected with H6N2. Tens of millions of birds in California became infected with this H6N2 virus during a four-month period beginning in March 2002."20

This massive epidemic—in contrast to the HPAI outbreak in Holland—was largely invisible. From the very beginning, growers used only their own veterinarians and did not release the diagnoses, "not to the state or to other potentially affected states, not to the OIE, not even to neighboring farms, who might have better protected their flocks from infection had they known about it." The emergence of this so-called "Triangle of Doom" was also kept quiet "by corporate decision-makers who feared that consumer demand would plummet if the public knew they were buying infected meat and eggs." As with the SARS outbreak in China the following year, economic interests trumped any concern for public health.

But what, exactly, is the human risk from H6N2? Carol Cardona, a University of California veterinary scientist, emphasizes that LPAI viruses all have the "potential to donate genetic material to potential pandemic strains. The interaction of animal agriculture and the public is complex and dynamic and we do not fully understand the risks associated with various types of contacts between humans and birds."22 Indeed, many researchers feel that the official between I.PAI and HPAI distinction outbreaks scientifically unsustainable and should not be allowed to dictate different levels of surveillance and response.<sup>23</sup> It is also imperative that agribusiness's bottom line not be allowed to supersede the global priorities of pandemic surveillance and human biosecurity. The bottom line: world public health cannot afford any holes or blind spots in the pandemic early warning system. As Robert Webster has advocated, the human-animal interface long needs comprehensive monitoring, with local public-health officials around the world supplied with a suitable kit of reagents to allow them to swiftly identify any influenza subtype.<sup>24</sup>

## **CHAPTER 6: PLAGUE AND PROFIT**

At the center of the meltdown in Asia's vast poultry industry is a 61-year-old multi-billionaire called Dhanin Chearavanont. 

1

Jasper Becker

All of today's tens of billions of highly engineered factory chickens are descended from red jungle fowl that still roam wild in forest regions of Thailand and Vietnam. Using mitochondrial DNA analysis, Japanese researchers in 1994 demonstrated that chickens were domesticated in the area of present-day Thailand more than 8,000 years ago. The chicken, along with the pig and the buffalo, subsequently became the basis of agrarian culture throughout Southeast Asia. Chickens are likewise the bottom line of Asia's largest and most powerful agricultural-export conglomerate, Bangkok-based Charoen Pokphand. CP, as it is universally known, figures centrally in the story of H5N1's terrifying return in the winter of 2003–4 and the unprecedented HPAI epidemic that threatens to become a global human and ecological cataclysm.

Founded by the immigrant Chia brothers from Guangdong, CP was a rice-seed distributor in Bangkok's Chinatown until Chia Ek Chow, the youngest of four sons,

took over the business in 1964. In the face of growing intolerance toward the Chinese diaspora throughout Southeast Asia, he changed his name to Dhanin Chearavanont and reoriented the company to chicken breeding and broiler farming. Impressed by the success of U.S. companies in transforming poultry raising into a streamlined industrial process more closely resembling traditional chemical manufacture than agriculture, Chearavanont formed two successive strategic partnerships with American companies and quickly became Asia's leading apostle of Tyson-style intensive farming and vertical integration.

By the mid-1990s, Thailand (which had adopted CP's corporate slogan, "Kitchen of the World,") had the most corporatized livestock industry in Asia. CP and a handful of other vertically integrated exporters controlled 80 percent of production, with chicken farming concentrated in a dense, polluted belt 60 to 150 kilometers outside Bangkok. With 100,000 employees across Asia, CP boasts that its agro-industrial empire is "fully integrated horizontally and vertically. Operations take in animal feed production, breeders, farming systems, meat processing, food production and its very successful value-added products."

For Chearavanont and other "integrators," economies of scale in a booming export environment have produced fabulous profits, but for CP's 10,000 contract farmers, as well as for hundreds of thousands of backyard poultry producers, the situation is radically different. As journalist Isabelle Delforge points out: "With contract farming, large companies control the whole production process: they lend

money to the farmers, they sell them chicks, feed and medicine, and they have the right to buy the whole production. But usually the company is not committed to buy the chickens if the demand is low. Contract farmers bear all the risks related to production and become extremely dependent on demand from the world market. They become factory workers in their own field." For the majority of Thai farmers, the Livestock Revolution has meant soaring indebtedness, loss of independence, and the continued migration of their daughters to Bangkok's sweatshops and brothels.

While Thailand's chickens (and later, pigs and prawns) have made Chearavanont a billionaire and, according to business magazines, one of the twenty most powerful businessmen in Asia, his central ambition has always been to honor his father's dream of bringing the Livestock Revolution—in the form of large-scale agro-industrial capitalism—back to China. Thanks to astute politicking and powerful Guangdong connections, CP was literally the first multinational investor to step foot inside Deng Xiaoping's "Open Door" in 1979 (CP's foreign business license in Shenzhen was number 001). In addition to holding a diversified portfolio of hotels, shopping malls, fast-food Kentuckv (including Fried franchises Chicken). telecommunications, and restaurants, it has built more than one hundred feed mills and poultry-processing plants throughout China in an attempt to forestall both foreign competitors (Tyson Foods, above all) and local upstarts in the world's most dynamic market for chicken products.

CP's explosive growth in Thailand and China, as well as its expanding operations in eighteen other countries, has required massive amounts of political grease. In 1996, for example, Chearavanont made an illegal \$250,000 donation to the Democratic National Committee in the United States, which backfired, causing bad publicity for both CP and the Clinton administration when fundraiser John Huang was indicted. The right-wing American Spectator pointed to CP's alliance with a leading Chinese weapon maker and implied that it was one of the "front companies for communist China" that had been "buying up (and spying on) the United States." But the magazine neglected to mention that a few months earlier, Neil Bush, George W.'s brother, had formed a joint venture company with Chearavanont. Indeed, as Dan Moldea and David Corn would later detail in the Nation, both the Bush family and the Carlyle Group—the private investment fund used by the family and other leading Republicans to turn insider access gold—have long-standing and intimate business relations with CP. Former president George H. W. Bush, for example, was reportedly paid \$250,000 by CP to lobby Asian and American leaders on its behalf.8

Chearavanont also acquired equity in the Thai state in 2001 with the appointment of his son-in-law Wattana Muangsuk as Deputy Commerce Minister. The cell-phone billionaire Thaksin Shinawatra—Siam's answer to Italy's Silvio Berlusconi—won the presidency that year with a lurid populist campaign. Thaksin's political party is called Thai Rak Thai, or "Thai Loves Thai," and he promised debt relief, cheap medical care, and a tough crack-down on drug

dealers (2,500 of whom, indeed, were promptly murdered by police death squads). In reality, explains economist Pasuk Phongpaichit, "His ascendency signifies a new consolation of big business and politics. Whereas the business people who have dominated Thai politics since parliament became significant in the 1980s used to be mostly provincial figures of only moderate wealth, Thaksin's government is controlled by the biggest Bangkok business groups to have survived the 1997 crisis." On the eve of the plague, in other words, Thailand was governed by a crony coalition of the telecommunications and livestock industries.

The return of avian influenza was shrouded in rumor, denial, and conspiracy during the fall of 2003. The epidemic actually began much earlier (Indonesia later conceded that H5N1 had been detected in August), but Chinese officials denied reports in the Hong Kong *Standard* that "farms throughout China [had] suffered from avian flu for several years." They also scorned rumors that there was a massive outbreak among ducks in Guangxi Province, bordering Vietnam, and likewise dismissed as Taiwanese propaganda the warning from Taipei that its animal inspectors in December had found H5N1 in wild ducks smuggled from Fujian, the province that was the likely source of the virus that killed two in early 2003. 11

In January 2004, the British magazine *New Scientist*, interviewing leading flu researchers off the record, created a small tempest with claims that the outbreak was the result of a clandestine and misguided vaccination campaign ("an uncontrolled experiment in viral evolution") by poultry producers in south China after the 1997 crisis in Hong

Kong. By using an inactivated virus to immunize their chickens, Chinese growers had actually accelerated the evolution of an H5N1 superstrain—genotype Z (GenZ)—that quickly became endemic but asymptomatic in domestic ducks. From this stable reservoir, it began to spread to other species via direct contact, poultry smuggling, and possibly by wild bird migration. 12

But Chinese authorities were not the only ones concealing the epidemic. In early November 2003, chickens started dying on farms across Thailand. As one farmer described it: "Their bodies began shaking; it was if they were suffocating, and thick saliva started coming out their mouths. We tried to give the hens herbs to make them better, but it made no difference. The faces then went dark green and black, and then they died." Although a veterinary scientist at Bangkok's Chulalongkorn University warned that he found H5N1 in several dead chickens, he was ignored by Thailand's Livestock Department. Likewise, when a worried farmer showed the carcasses of his dead flock to an official, he was told that the birds had died "without any medical cause." 14

Strangely, in the midst of all these bird deaths, the corporate chicken-processing plants were working overtime. As angry trade unionists at one factory just outside the capital told the *Bangkok Post* after the scandal broke: "Before November we were processing about 90,000 chickens a day. But from November to 23 January, we had to kill about 130,000 daily. It's our job to cut the birds up. It was obvious they were ill: their organs were swollen. We didn't know what the disease was, but we

understood that the management was rushing to process the chickens before getting any veterinary inspection. We stopped eating [chicken] in October."<sup>15</sup>

The wall of official silence across Asia was breached in December when chickens started dying en masse on a farm near Seoul. Korean agricultural officials were stunned to discover H5N1, but, in contrast to their counterparts in China and Thailand, they promptly notified the Office International des Epizooties (OIE); a week later, South Korea announced a massive cull after new infections were identified in chicken and duck flocks in five provinces. Meanwhile children, not just chickens, had been dying mysteriously in Vietnam; just before the New Year, one of the CDC's influenza experts in Atlanta received a worried email from a virologist in Hanoi, which described patients suffering from symptoms of viral pneumonia and acute respiratory distress syndrome (ARDS), which had caused the death of many of the 1918 pandemic's victims.

The Hanoi doctor and her colleagues were unaware that their own agriculture bureaucracy had been concealing, at least since October, evidence of a sporadic H5N1 epidemic among poultry. On January 5, 2004, following the deaths of several more people, Vietnamese public-health officers urgently requested help from the WHO, whose regional office in Manila also soon heard rumors as well of Vietnam's HPAI outbreak; a few days later Hong Kong experts confirmed that the Frankenstein GenZ had been found in forensic samples from three of the dead children in Hanoi. Simultaneously, Vietnam officially acknowledged an avian flu epidemic in two provinces and Japan announced the

discovery of H5N1 among hens in Yamaguchi Prefecture. (The outbreak in western Japan had originally been concealed by poultry company officials—one of whom later committed suicide—and only came to light thanks to an anonymous tip-off from a company employee.)<sup>17</sup>

The WHO and its veterinary counterpart, the OIE, as well as the UN Food and Agricultural Organization (FAO), were horrified to realize that bureaucrats and agribusiness spokespeople had for months been covering up an avian flu epidemic of continental scope. Facing an increasingly cynical world press, it became almost impossible for the international agencies to accept the reassurances that continued to flow from Chinese and Thai ministries—the Chinese, in particular, seemed to have reverted to the Orwellian culture of secrecy and deception previously associated with the Jiang Zemin camp. When another mystery respiratory infection swept Guangdong in January 2004, officials dismissed it (shades of SARS) as the bacterium *Chlamydia pneumoniae* and refused to let the WHO investigate on the spot. 18

In Thailand, meanwhile, lies were being manufactured almost as fast as sick chickens were being slaughtered and shipped to overseas markets. Deputy Minister of Agriculture Newin Chidchob talked nonchalantly about a few cases of "avian cholera," while Prime Minister Thaksin and his ministers, to assuage a nervous public, "devoured a big feast of deliciously cooked, Thai-style chicken dishes in a nationwide television broadcast." CP senior executive Sarasin Viraphol assured reporters that, although the company would not allow the press to inspect its plants,

avian flu was completely absent in Thailand. In fact, as the Bangkok press later reported, the government had been colluding with CP and the other giant poultry producers to conceal the epidemic by paying contract farmers with infected flocks to keep quiet; official deceit gave the big exporters several months to process and sell diseased inventory, as well as to disinfect their plants and institute isolation procedures in their battery warehouses. Small producers, however, were left alone to bear the brunt of the epidemic's human and economic costs.<sup>20</sup>

Finally, in late January, with two young farm boys critically ill from influenza, the Thai parliamentary opposition, led by maverick senator Nirum Phitakwatchara, was able to force Prime Minister Thaksin Shinawatra to admit that H5N1 was, in fact, ravaging the poultry belt. His staff immediately off-loaded responsibility for official mendacity onto lowly provincial officials. "What looks like a cover-up," Thaksin's spokesman deadpanned, "was a misinterpretation of procedures. The most appropriate word is 'screw-up.' Some agencies screwed up."<sup>21</sup>

Small producers, in response, screamed that "by denying the facts, the government was helping out the major operators, but in the end it's us small farmers who are suffering."<sup>22</sup> A Bangkok newspaper contrasted the fate of big and small poultry producers in Sukhothai Province. The commercial growers "integrated" by CP and other conglomerates were notified about the epidemic in December and were provided with antiviral vaccines by livestock officials, and thus their inventories were saved. But small-holders were kept in the dark about the disease,

and as a result most of their chickens perished as did one peasant's teenage son. 23

The EU, Japan, and South Korea promptly embargoed Thailand. imports while from the poultry administration, grateful for Thaksin's support of U.S. interventions in Afghanistan and Iraq, avoided public criticism of the cover-up. CP's stock immediately fell by an eighth, and the ground shook. ("In Thailand," writes Isabelle Delforge, "when CP sneezes, the whole business community catches cold—or flu.")<sup>24</sup> Dhanin Chearavanont, however, was surprisingly upbeat and urged Thais to "turn the crisis into opportunity." The plague, in other words, might rationalize poultry production. But opportunities and benefits for whom? The government quickly unveiled a sweeping plan to complete the modernization of the Thai poultry industry by culling small-scale, open-air flocks and requiring their operators to build new industrial poultry houses; only those farmers who fully complied with the plan would be eligible for compensation for their dead chickens.

Thailand's agrarian populists, including senator and agricultural economist Chirmsak Pinthong, promptly denounced the government's plan as another cunning move by Chearavanont to force the small operators into the extinction or turn them into serfs of CP.<sup>25</sup> Smallholders complained that government compensation for their dead chickens was only a fraction of what CP and others were charging them to restock their flocks. There was also evidence that the poultry cull was being used to strengthen the corporations. "When the avian flu was detected," writes Delforge and a Thai colleague, "a red zone was cleared

around the farm and all the poultry in the zone were killed to prevent the spread of the disease. However, some farmers reported dead chickens but no red zone was declared around their property. They suspected the authorities of protecting neighboring industrial farms or owners of highly valuable fighting cocks."<sup>26</sup>

He Changchui, FAO assistant director-general and regional representative for Asia and the Pacific, indirectly criticized the giant producers by stressing the role of "high densities of humans and animals ... [in] creating new pathways for disease transmission through inappropriate waste disposal, direct contact or through airborne transmission." He urged a "substantial restructuring" of poultry production along lines that favored the poor, protected the environment, and compensated the small outbreak.<sup>27</sup> producers affected by the The Thaksin uncritically however. embraced government, Chearavanont's contention that avian flu's spread was due to the small producers and their "backward" open-air chicken flocks. CP claimed that its industrialized, enclosed farming system was virtually impregnable to viral outbreaks and epidemics.

While it is true that Southeast Asia's traditional backyard chicken flocks offer myriad opportunities for infectious interchange between different species of poultry and wild birds, the huge chicken factories (50,000 birds per two-story structure) maximize the accumulation of viral load and subsequent antigenic drift. In an epidemiological sense, the outdoor flocks are the fuse, and the dense factory populations, the explosive charge. As *Vietnam News* 

reported on February 4, 2004, "The army has been mobilized to kill 117,000 birds on the biggest farm in Ha Tay province, owned by the Thai Charoen Pokphand Company."  $^{29}$ 

Once the Thais had publicly acknowledged their outbreak, the other major deceivers—Indonesia and China — were forced to play show-and-tell as well. The scandal of Indonesia's February 2 confession that the government had been concealing knowledge of an H5N1 outbreak since late August was compounded by Agriculture Minister Bungaran Saragih's extraordinary explanation that they had withheld information because "we did not want to cause unnecessary losses through a hasty decision." 30

Chinese officials managed to be even more arrogant and egregious in their attempt to save face than their Indonesian counterpart. In the first week of February they grudgingly doled out in bits and pieces the admission that H5N1 was raging in no fewer than twelve provinces and cities, including Guanxi, Guangdong, and even metropolitan Shanghai. Ten days later, Chen Kaizhi, a top official in Guangzhou, demonstrated the stunning scientific ignorance of senior bureaucrats like himself in a speech to the Guangdong People's Congress: "This disease is hundreds of years old and it can be prevented and treated. Vaccines are effective. No humans have been infected, so why this uproar?" Chen went on to contrast the hysteria of Hong Kong health officials, the WHO and other "outsiders" with traditional folk wisdom. "In the past when life was hard, we hoped for a disease among our chickens so that we got to eat chicken. When a chicken at home dropped its head, we

said, 'good, now we get to eat chicken.' Now we are so advanced that people are not allowed to eat diseased chicken."

31

Chen, of course, ignored the fact that, thanks to the cover-ups in Guangdong and elsewhere, thousands of people had consumed diseased chicken products. Meanwhile, the Hong Kong media that had earlier reported suspected cases in the PRC or now dared to criticize the ignorance of officials like Chen were threatened with legal action under the same infamous mainland statute that had been used to suppress reportage of SARS a year earlier.

While observers speculated about what had happened to of short-lived reign scientific and the medical "transparency" in China, the OIE and WHO were desperately worried about the haphazard, and, in some cases, perfunctory character of the poultry culls that were Asia's only hope of containing the H5N1 catastrophe. In Thailand, where prisoners were mobilized under army supervision to bury millions of chickens alive, the flocks of producers, as we have seen. were dutifully massacred, while corporate chickens received special treatment. Activists charged that "workers and consumers' health clearly comes after exporters wealth," and the WHO scolded the government for its lackadaisical attitude toward protecting farmers and cullers from infection. authorities also wasted valuable time in the needless slaughter of wild birds and urban pigeons after Prime Minister Thaksin, in characteristic xenophobic fashion, blamed "foreign" wildfowl for starting the epidemic. 32

Table 2: Covering Up the Epidemic

Country	Official Admission	Actual Onset
S. Korea	12/12/03	
Vietnam	1/8/04	10/03
Japan	1/12/04	
Thailand	1/23/04	11/03
Cambodia	1/24/04	
China	1/27/04	early 2003
Laos	1/27/04	
Indonesia	2/2/04	8/03

The government of Vietnam, previously praised by the WHO for its competent handling of the SARS outbreak, was altogether more cooperative, but the country's poverty and the dispersed character of its largely backyard poultry industry posed huge obstacles to creating effective viral firebreaks. Poor farmers suppressed news of infections and concealed valuable birds such as fighting cocks; in addition, in face of rising anger in the countryside, the government was reluctant to extend the radius of culls around sick flocks beyond one half kilometer—the WHO recommended three kilometers—or to exterminate the domestic ducks that were the infection's probable reservoir. Similarly, the disinfection of farms and the disposal of contaminated poultry manure were Sisyphean tasks that always risked further transmission of the virus, typically via the boots or clothing of cleanup workers. No sooner was an outbreak suppressed in one part of the country than another

appeared in a different province. Small children, who frequently played outside with chickens and ducks and were constantly exposed to poultry waste, were particularly vulnerable to these seemingly ineradicable village outbreaks. 33

president Indonesian Megawati Sukarnoputri, meanwhile, balked at the task of killing millions of chickens, and so her government initially proposed a vaccination campaign instead. After angry protests from the rest of the ASEAN bloc, Indonesia finally agreed to slaughter birds, but with a halfheartedness that reassured few critics. The WHO, however, continued to have the most difficulty with Beijing. "We have repeatedly said there is a brief window of opportunity to act within China," warned a WHO representative at the beginning of February 2004. "This latest news [outbreaks in Hunan and Hubei] strongly suggests that the window is getting smaller with each passing day." 34 The Lancet, for its part, warned in February that China's "animal-disease surveillance is as good as absent, a vacuum into which global health might hopelessly and terrifyingly fall."35

February was, indeed, a terrifying month, with new human victims in Vietnam and Thailand and further avian outbreaks in China and Indonesia. WHO teams, reinforced with a cadre of top experts from American, European, and Japanese laboratories, struggled with the imminent possibility of a global pandemic against which the world would have little protection. An experimental vaccine developed in 1997 was ineffective against GenZ, which was

also resistant to amantadine, the cheapest and most common antiviral.  $\frac{36}{}$ 

Most disturbingly, the new strain was more lethal than any influenza in scientific experience. In the course of the viral pneumonia it engendered, GenZ was stunningly adept at inducing deadly "cytokine storms" in which victims' own berserk immune systems destroyed their lungs and other organs; two-thirds of GenZ's victims (twenty-two out of thirty-three) had died by March 9, and, unlike its 1997 cousin, it relished toddlers and teenagers as well as adults.37 With each passing day, scientists feared they would meet its reassortant offspring, ready to conquer the world, but despite their repeated warnings only one undertaken country—Canada—had truly serious preparations to meet the pandemic threat. 38 In the meantime, only the dismal, dirty work of the slaughter some 120 million chickens were eventually buried alive, burnt to death, electrocuted, or gassed—offered any hope of preventing a fatal rendezvous between a nightmare virus and a vulnerable humanity.

Then in mid-March, the plague suddenly seemed to relent. On March 16, China announced that it had eradicated the virus in all forty-nine hot zones; this triumphalist statement alarmed the FAO and the OIE, who cautioned against premature declarations of victory—the international protocol was to carefully monitor flocks for six months before ruling that a region or nation was free of avian influenza. The international agencies warned that the crisis was not over, and they warned countries not to restock poultry until they had adequate surveillance and

biosecurity in place. 39 Nonetheless, Vietnam followed China's example on March 30 and declared the outbreak over.

Thailand also intimated that it was making splendid progress and would soon join the ranks of the victors. Somehow, despite the cover-ups, official lies, and months of lost ground, and despite the bungled culls and the gaping holes in the influenza surveillance network, the great chicken slaughter nevertheless seemed to have turned the tide. The WHO's warnings about an imminent pandemic seemed less urgent, and the more optimistic, especially the politicians and exporters, thought they had defeated H5N1. But alas, the virus had simply taken a brief vacation.

## CHAPTER 7: EDGE OF THE ABYSS

Pandemic? Very, very likely. 1

WHO regional director for Asia

The economic impact of the avian flu epidemic on the Southeast Asian countryside was profound. Thousands of small chicken farmers were bankrupted and forced out of business, thus yielding ground, as Chearavanont had urged, to the corporate operators. Meanwhile, the unprecedented market turbulence unleashed by the H5 epidemic in Asia, by the North America, H7 outbreaks in followed encouraged the big poultry producers to poach one another's customers. In the United States, giants like Tyson and Pilgrim's Pride were "already reaping some benefits from the bird flu virus" in late January as they rushed exports to replace the quarantined Thai supply. CP, meanwhile, exploited its own disaster by increasing exports from plants in Taiwan and other nonembargoed countries to take advantage of the sharp rise in chicken prices. To offset current and future EU import controls, Chearavanont also announced an ambitious expansion of poultry operations in Romania, Russia, and Ukraine, and he reassured his shareholders that they would soon reap profit from the

influenza-driven restructuring of global chicken production.<sup>2</sup>

All of this cheery news from the giant chicken producers was of little solace to the researchers struggling to understand the spectacular menace of H5N1 GenZ. An extraordinary research consortium combining the resources of Robert Webster's St. Jude Hospital group, the veteran team from the University of Hong Kong, and local experts from across Asia had been working feverishly to unravel the genealogy and molecular structure of the 2003–4 strain. Their findings were disturbing.

In a letter to *Nature* in July 2004, they warned the virus's erstwhile conquerors that, in fact, avian flu—now comfortably ensconced among asymptomatic domestic ducks—was almost ineradicable. "H5N1 is now endemic in poultry in Asia and has gained an entrenched ecological niche from which to present a long-term pandemic threat to humans." Moreover, its sudden retreat in March might have had more to do with influenza's seasonal cycle than with the mass murder of chickens.<sup>3</sup>

Although they now possessed a detailed map of the structure of GenZ—each protein had been analyzed to the last amino acid group—they were still baffled by its functional organization: they had, so to speak, a splendid view of the wiring, but only a fragmentary concept of its purpose. They knew that GenZ, the sole survivor of a marathon competition between more than a dozen H5N1 genotypes, was a superfit strain, and was evolving rapidly as it passed back and forth between different populations and species. They also knew that natural selection,

horrifyingly, seemed to favor increased virulence in humans, but they were unable to nail down the molecular determinants of the human infections in Vietnam and Thailand or, for that matter, explain why H5N1 had not yet acquired pandemic transmissibility.<sup>4</sup>

Just as researchers feared, GenZ came creeping back at the end of spring, infecting a mixed flock of chickens and waterfowl at a university research farm in Thailand in late May; by July there were widespread outbreaks in Vietnam, central Thailand, and China's Anhui Province. Thai officials again responded by blaming foreign birds and ordered crews to exterminate open-bill storks and chop down the trees they nested in.<sup>5</sup> In mid-August veterinary officers discovered Malaysia's first case of H5N1 in a pair of fighting cocks returned from a match in Thailand: troubling evidence that the prized sporting birds were now a vector of infection. Vietnam then shattered hopes with a belated announcement that three people, including two young sisters, had died between July 30 and August 3 in Hau Giang Province, southwest of Ho Chi Minh City.<sup>6</sup>

Bad news grew worse in September with human deaths reported in Thailand, the first being a eighteen-year-old game-bird trainer. Over the next two weeks an eleven-year-old girl and a thirteen-year-old boy died, while nine other children languished in intensive care. Dr. Shigeru Omi, the WHO's regional director for the Western Pacific Region, warned emphatically in mid-September that "unless intensified efforts are made to halt the spread of the virus, a pandemic is very likely to occur." In an oafish attempt to reassure international opinion that his government was on

the job, the director of the Department of Livestock Development, Yukol Limlamthong, emphasized that avian flu outbreaks had been identified in "only 56 locations across 23 provinces ... not hundreds of spots as in some news reports." The exasperated head of the Public Health Ministry, Dr. Charal Trinwuthipong, promptly blasted Limlamthong's department for its negligence in monitoring and reporting outbreaks: "They've not improved! How damned lousy they were last time, that's how they still are." §

While the fur was flying between Thai ministries, simultaneous outbreaks of H5N1 and H3N2 in several districts in Thailand again raised the specter of pandemic reassortment. Despite pleas from leading public-health experts, Prime Minister Thaksin refused to import vaccine from Europe to protect the country's exposed populations. He did, however, robustly defend CP against embarrassing charges by Cambodian farmers that chickens purchased from CP Cambodia Ltd. were the source of a new outbreak in that country. He also proposed to aid the big exporters by bartering their contaminated chicken to Moscow. He ordered his ambassador in Moscow to offer a mountain of chicken in exchange for Sukol SU-30 fighters for the Thai air force. Vladimir Putin, unsurprisingly, declined to accept the bargain. 10

All this, however, was just a bizarre prelude to the devastating news revealed to the world by the WHO on September 28: Pranee Thongchan in Kamphaeng Phet was the first victim of a probable human-to-human transmission of the virus, which she contracted from her mortally ill

daughter (see Preface). Although Klaus Stohr, the former East German veterinarian who was now head of the WHO Global Influenza Program, reassured the public that the case was epidemiologically a "nonsustained, inefficient, dead-end street," CDC scientists were, in fact, frantically sequencing viral samples from the dead mother and daughter to see if GenZ had "mutated significantly— or worse, reassorted with a human flu"—a possible consequence of the government's failure to vaccinate hotspot populations. In a joint statement, the WHO and FAO warned that avian influenza was now "a crisis of global importance." 11

Although no human flu genes were found in the viral samples, Pranee's death was an earthquake that thoroughly shook international confidence in Thailand. More than chicken exports were now endangered: tourism, the source of 6 percent of the nation's GDP, was under threat. Prime Minister Thaksin responded with a tantrum in which he blamed the "ignorance" of villagers for the persistence of the outbreak and—music to the ears of corporate poultry producers—threatened to ban farm families from raising fowl in their yards. He melodramatically ordered his ministers to eradicate the flu in a month or lose their heads. And facing charges that livestock authorities were bungling the monitoring of poultry, he called for a million volunteers to search the country for sick chickens. 12

Thaksin's crusade against small farmers and wild birds, however, did not prevent further deaths. Neighbors of nineyear-old Kanda Siluangon, who died in early October, "blamed district and provincial livestock officials, saying they did nothing for one month after being notified of the chicken deaths." <sup>13</sup> A female worker at a chicken-processing plant died a few days later, followed in mid-October by a fourteen-year-old farm girl. The most unexpected victims in October, however, were cats, big and small. As their horrified keepers stood helpless, more than eighty Bengal tigers at the famed Sriracha Tiger Zoo near Bangkok perished in spasms of viral pneumonia. They had been fed raw chicken. <sup>14</sup>

There was no shortage of dismaying visions in the late When Newsweek fall 2.004 asked a microbiologist whether a pandemic was possible, he replied, "I don't think we completely understand why it hasn't happened already." Indeed, there was broad agreement among researchers that an H5 pandemic was not simply imminent, it was "late." Getting this urgent message across to news media, the nonspecialist medical community, NGOs, and ultimately, to presidents, prime ministers, and kings the world over was the urgent task entrusted to the WHO (in theory, the medical conscience of and humanity). It was an uneven divided compromised by undue deference to the interests of powerful states, including China and the United States, which generated some lurid headlines and rhetorical promises but none of the truly decisive action urged by experts on the ground.

Many researchers and activists wondered if the WHO was not being too meek in sounding the tocsin. In particular, they worried that WHO's influenza czar, Klaus Stohr, had been deliberately underselling the menace of

H5N1 in order to safeguard the organization's credibility in the face of skeptical governments. When asked about possible mortality, Stohr routinely referred to a U.S. CDC study that projected 2 to 7.4 million deaths globally, but CDC health economist Martin Meltzer had derived these figures by extrapolating from the mild 1968 pandemic; most influenza experts actually feared that H5N1 could become as deadly as the 1918 virus. Michael Osterholm, the respected director of the Center for Infectious Disease Research and Policy at the University of Minnesota, characterized Stohr's cautious estimates as "rather ridiculous." <sup>16</sup>

Table 3: How Many Might Die?

1957 mortality	2 million
1968 mortality	0.7 million
1968 extrapolated (Stohr)	2 to 7.4 million
1918 mortality	40 to 100 million
Omi's estimate	7 to 100 million
1918 extrapolated	325 million (maximum)
H5N1 mortality extrapolated	1 billion

Most of the scientific community, therefore, was heartened when the WHO's Shigeru Omi evoked the 1918 precedent when he warned the press on November 29: "We are talking at least seven million [deaths], but maybe more—10

million, 20 million and the worst case, 100 million." (Omi was still being conservative: an direct extrapolation of maximum 1918 mortality to today's world population would be 325 million dead.) The cat was out of the bag, and top experts, like Malik Peiris at the University of Hong Kong, rushed to defend Omi's figures as "consistent with current research."

The WHO ultimately bowed to majority opinion and, over Stohr's objections, revised his previous estimates as "a best-case scenario"; 50 million dead was now officially the "worst case." Yet a few epidemiologists think even 50 million dead is wishful thinking. Extrapolating from the current lethality of GenZ rather than from 1918 mortality (i.e., 72 percent versus 2.5 percent), they reminded officials that the true worst-case scenario, in fact, was more in the range of *1 billion* deaths. 17

## CHAPTER 8: HOMELAND INSECURITY

Regardless of human endeavors, nature's on-going experiments with H5N1 influenza in Asia and H7N7 in Europe may be the greatest bioterror threat of all.  $^{1}$  Richard Webby and Robert Webster

On December 3, 2004, U.S. secretary of Health and Human Services (HHS) Tommy Thompson held a press conference to announce his resignation. His turbulent, heavy-handed reign had alienated most of the leading disease researchers at the National Institutes of Health (NIH) and elsewhere.<sup>2</sup> Unlike the previous seven cabinet members purged in President Bush's postelection housecleaning, Thompson, according to the New York *Times*, "gave unexpected answers to questions posed to him." He complained, for instance, that Congress, ever solicitous of the pharmaceutical industry, had refused to give him authority to negotiate lower prices for Medicare prescriptions. He also agreed with FDA critics that an independent watchdog of the agency was needed in the wake of scandals about the safety of Vioxx and other drugs. "Asked what worried him most, Mr. Thompson cited the threat of a human flu pandemic.... 'This is a really huge

bomb that could adversely impact on the health of the world,' killing 30 million to 70 million people, he said."

The secretary, of course, spoke with the authority of someone with access to the best medical intelligence in the world, but reporters were undoubtedly surprised that so alarmed about a peril that his Thompson was department with its \$543 billion annual budget—a guarter of the federal total—had done so little to address. In the last fiscal year, for example, Thompson had allocated more funds to "abstinence education" than to the development of an avian influenza vaccine that might save millions of lives. This is but one example of the way that all Americans, but especially children, the elderly, and the uninsured, have been placed in harm's way by the Bush regime's bizarre skewing of public-health priorities. On Thompson's watch, HHS and the Pentagon spent \$14.5 billion to safeguard national security against largely hypothetical biological threats like smallpox and anthrax, even as they pursued a penny-pinching strategy to deal with the most dangerous likely "bioterrorist": avian influenza. The administration's lackadaisical response to the pandemic threat (despite Secretary Thompson's personal anxiety) is only the tip of the iceberg. Over the last generation, writes Lancet editor Richard Horton, "The U.S. public-health system has been slowly and quietly falling apart."5

Under Democrats, as well as Republicans, Washington has looked the other way as local health departments have lost funding and crucial hospital surge capacity has been eroded in the wake of the HMO revolution. (A sobering 2004 Government Accounting Office [GAO] report

confirmed that "no state is fully prepared to respond to a major public-health threat.")<sup>6</sup> The federal government also has refused to address the growing lack of new vaccines and antibiotics caused by the pharmaceutical industry's withdrawal from sectors judged to be insufficiently profitable; moreover, revolutionary breakthroughs in vaccine design and manufacturing technology have languished due to lack of sponsorship by either the government or the drug industry.

Reagan-era medical priorities were cancer and heart disease—"middle-class" health issues with broad electoral resonance—rather than infectious disease or community-based medicine; as a consequence, savage federal cutbacks in the early 1980s led the Institute of Medicine to warn in 1987 that the United States was ill-prepared to face the threat of emergent diseases. The Institute declared: "The decline in preparedness and effectiveness of the nation's first-line medical defense systems can be traced to these ill advised budget cuts which forced the termination of essential and research and training programs."

There was great hope that the Clinton administration with its strategic focus on health-care reform would finally re-arm the country to adequately face the new viral perils, but as writer Greg Behrman recounts in his bitter history of how Washington "slept through the global AIDS pandemic," Clinton public-health policy was undermined by the administration's own fetishism of deficit reduction, followed by the Republican capture of Congress in 1994.<sup>8</sup> To her credit, Donna Shalala, Clinton's HHS secretary, did establish a pandemic influenza planning process in 1993,

with the National Vaccine Program Office (NVPO) as the lead agency. After the 1997 Hong Kong outbreak, to which the CDC was a major responder, Shalala ordered NVPO to prepare technical content for a federal response plan. Much of this, however, was simply bureaucratic rewiring that provided little incentive for vaccine development or reinvestment in local public-health agencies.

In October 2000, the GAO scolded HHS for making so little progress in the development of an avian flu vaccine. It warned that the United States might only have a month (or less) of warning before a pandemic became widespread, and it accused HHS of failing to develop contingency plans to ensure expanded vaccine manufacturing capacity. It also pointed to a major contradiction in business-as-usual reliance on the private sector: "Because no market exists for vaccine after [flu season], manufacturers switch their capacity to other uses between about mid-August and December." At minimum, HHS needed to find some way to keep production lines running full-time, all year long, as well as to diversify the number of companies committed to vaccine production. In addition, the GAO slammed HHS for dithering over whether or not to stockpile antivirals, even as top influenza experts were begging the government to much oseltamivir (Tamiflu)—the "miracle" procure as neuraminidase inhibitor—as possible. Almost eight years of "process," the GAO report implied, had failed to achieve a "plan" in any substantive or meaningful sense. 9

Meanwhile, the Republican leadership in Congress, after driving a silver stake through Clinton's health insurance reform, slashed at programs that even faintly smacked of

social entitlement. Federal funding for state immunization programs (which Clinton had dramatically increased) was a principal target, with aid cut in some cases by more than 50 percent. As a 2000 study by the National Institutes of Health (NIH) emphasized, influenza vaccination already lagged far behind its potential to prevent disease and death. NIH pointed to glaring racial and income disparities in flu vaccine coverage, attributing the low vaccination rates among blacks (22 percent), Latinos (19 percent), and the uninsured (14 percent) to federal cutbacks, as well as the increased dependence of Americans upon tightwad HMOs for their medical care. 10 Another researchers at the University of Rochester found that only 39 percent of black people over age sixty-five received influenza vaccinations as compared with 71 percent of white seniors. 11 There was—and is—still a color line in prevention of flu mortality.

The restructuring of health care around HMOs, with the attendant closure of hundreds of hospitals across the United States, had left many big cities without the capacity to deal with abnormal spikes in patient loads; the HMO ideal was to ruthlessly reduce the number of unused, and thus unprofitable, hospital beds to zero: an example of "just-in-time" management gone berserk. Public hospitals, meanwhile, were caught between their chronic budgetary problems and soaring demand by the more than 40 million poor and uninsured Americans. A 2003 survey by the American College of Emergency Physicians found that 90 percent of the country's 4,000 emergency departments

were seriously understaffed and overcrowded, with little surge capacity. 12

After the 2002 election the Institute of Medicine looked back glumly at the Bush senior and Clinton epochs. It found that many of its past recommendations had never been implemented and that the public-health system "that was in disarray in 1988 remains in disarray today." 13 This "disarray," including all the flaws in HHS's influenza program (particularly the lack of an antiviral stockpile and adequate vaccine manufacturing capacity), was inherited by Tommy Thompson, the former governor of Wisconsin, described as a "pragmatic conservative" by his friend Ted Kennedy. The Clinton administration's handling of publichealth issues had certainly been disappointing, but the new Bush administration was frightening to everyone who had been fighting to prevent the total meltdown of urban public health. Then, in September 2001, a new dispensation suddenly arrived in the form of poisoned letters contaminated with "weaponized" anthrax. DNA sequencing would later reveal that the anthrax strain used in the attacks almost certainly originated from the Army's own laboratory at Fort Detrick, Maryland, yet this probable "inside job" became the principal justification for national hysteria about the threat of "bioterrorism" supposedly posed by Iraq, al-Qaeda, and other alien enemies of the United States. 14

With shockingly little debate and without any real evidence that such a threat even existed, most public-health advocacy groups, as well as such leading Democrats as John Edwards and Ted Kennedy, became ardent shareholders in

the bioterrorism myth. Even the liberal Trust for America's Health glibly talked of an "Age of Bioterrorism" as if malevolent hands were already opening little vials of botulism and Ebola on Main Street. In fact, the irresistible attraction of the so-called "health/security nexus" was the billions that the White House was proposing to spend on Project BioShield, Bush's "major research and production effort to guard our people against bioterrorism." Many wellmeaning people undoubtedly reasoned that, however farfetched the excuse, the Republicans were finally throwing money in a worthwhile direction and that some of the windfall would surely find its way to real needs after decades of neglect. Because the defensive preparations against bioterrorism borrowed heavily from pandemic planning, there was hope that influenza (previously shortchanged in the design of the National Pharmaceutical Stockpile in 1999) would be accorded its proper rank as a "most wanted" bioterrorist.

Certainly the leading influenza researchers, from 2001 onward, were doing their utmost to alert medical colleagues worldwide to the urgent threat of avian flu, as well as outlining the immediate steps that the Bush administration and other governments needed to take. As befitted his position as "pope" of influenza researchers, Robert Webster tirelessly preached the same sermon: "If a pandemic happened today, hospital facilities would be overwhelmed and understaffed because many medical personnel would be afflicted with the disease [the lesson of SARS]. Vaccine production would be slow because many drug-company employees would also be victims. Critical

community services would be immobilized. Reserves of existing vaccines, M2 inhibitors, and NA inhibitors would be quickly depleted, leaving most people vulnerable to infection."<sup>15</sup>

Webster stressed the particular urgency of increasing production of the neuraminidase (NA) inhibitor oseltamivir (Tamiflu). Because a vaccine was unlikely to be available in the early stages of a pandemic, Webster urged that "NA inhibitors [e.g. oseltamivir] should be stockpiled now, in huge quantities." Because this strategic antiviral was "in woefully short supply"—made by Roche at a single factory in Switzerland—Webster and his colleagues underlined the need for resolute government action. Failure to act would mean intense competition over the small inventory of lifesaving Tamiflu. "Who should get these drugs? Health-care workers and those in essential services, obviously, but who would identify these? There would not be nearly enough for those who needed them in the developed world, let alone the rest of the world's population." 16

Webster was not calling for a new Manhattan Project, just prudent action to ensure an adequate antiviral stockpile. But for almost three years he and other influenza experts were ignored, as were those who argued more generally that "the best way to manage bioterrorism is to improve the management of existing public health threats." The Bush administration instead fast-tracked vaccination programs for smallpox and anthrax, based on fanciful scenarios that might have embarrassed Tom Clancy. In reality, Project BioShield was designed to build support for the invasion of Iraq by sowing the baseless fear that

Saddam Hussein might use bioweapons against the United States. In any event, Washington spent \$1 billion expanding a smallpox vaccine stockpile that some experts claim was already quite sufficient. Hundreds of thousands of GIs were forced to undergo the vaccinations, but frontline health workers—the second tier of the smallpox campaign—largely boycotted the administration's attempts to cajole "voluntary" participation.

In spite of this fiasco and millions of doses of unused administration pressed ahead with the vaccine, the development of second-generation smallpox and anthrax vaccines, as well as vaccines for such exotic plagues as Ebola fever; it continued to reject the "all hazards" strategy recommended by most public-health experts in favor of a so-called "siloed approach" that focused on a shortlist of possible bioweapons. In testimony before the House of Representatives, Tommy Thompson explained that while "private investment should drive the development of most medical products," only the government was in a position to develop those products that "everyone hopes ... will never be needed" as a protection against "rare yet deadly threats." As Project BioShield morphed into the biggest show in town (growing from \$3 billion in fiscal 2002 to more than \$5 billion in fiscal 2004), Thompson's wayward logic soon had perverse impacts that confounded the hopes of the biodefense boom's early enthusiasts. 18

For example, instead of spurring a welcome trickle-down of money for research on big killers like influenza, malaria, and tuberculosis, BioShield stole top laboratory talent away from major disease research. Reporting on this new "brain drain," writer Merrill Goozner cited the case of a leading UCLA lab that phased out its "basic science research on TB in favor of studying tularemia [rabbit fever]"—a disease that "has zero public-health importance"—because the latter infection was "on the government's A-list of potential bioterrorism agents" and tuberculosis was not. [19] (After workers at a different lab accidentally infected themselves with tularemia, some scientists expressed concern to the New York Times that "leaky" biodefense research "may pose a menace to public health comparable to the still uncertain threat from bioterrorism.") [20]

To many infectious disease experts, Project BioShield was Bush's and Thompson's version of *Through the Looking* Glass, with priorities established in inverse relationship to actual probabilities of attack or outbreak. "It's too bad that Saddam Hussein's not behind influenza," complained Dr. Paul Offitt, a dissident member of the government's advisory panel on vaccination. "We'd be doing a better job."21 Indeed, HHS's zeal to combat hypothetical bioterrorism contrasted with its incredible negligence in exercising oversight over the nation's "fragile" influenza vaccine supply. As the GAO had warned Donna Shalala, vaccine availability in a pandemic would depend upon the stability and surge capacity of existing production lines. But as shocked Americans discovered in the winter of 2003-4 and again in the early fall of 2004, the entire vaccine manufacturing system had decayed almost to the point of collapse.

"Big Pharma," as recent exposés have emphasized, is the most profitable industry in the United States, and it maintains the most powerful lobby on Capitol Hill.<sup>22</sup> Thanks to the tolerance of a Congress awash in its campaign contributions, the drug industry mines gold from outrageous prescription prices for drugs that manage chronic illness (diabetes, high blood pressure, asthma, and so on), as well as the sale of such lifestyle enhancers as Viagra.

Products that actually cure or prevent disease, like vaccines and antibiotics, are less profitable, so infectious disease has largely become an orphan market. As industry analysts point out, worldwide sales for all vaccines produce Pfizer's than income revenue from anticholesterol medication. 23 Despite the 90,000 Americans who die every year from hospital infections, the drug corporations also spending scorn money development of new antibiotics. Indeed, as Nature writer Martin Leeb points out, "from a marketing standpoint, antibiotics are the worst sort of pharmaceutical because they cure the disease."24 The giants prefer to invest in marketing rather than research, in rebranded old products rather than new ones, and in treatment rather than prevention, in fact, they currently spend 27 percent of their revenue on marketing and only 11 percent on research. "Preventing a flu epidemic that could kill thousands," wrote Donald Barlett and James Steele in *The New York Times*, "is not nearly as profitable as making pills for something like erectile dysfunction."25

# CHAPTER 9: STRUCTURAL CONTRADICTIONS

One of the most difficult things to explain to the public after a pandemic would be why we weren't prepared, because there have been enough warnings. 1

Klaus Stohr, WHO

are especially disliked by drug Influenza vaccines companies because they are tricky to produce, become obsolete after one season, and are subject to large fluctuations in demand. Moreover, the basic production process has changed little since the days of Francis and Salk a half century ago, and the industry has failed to invest in the faster and safer cell-culture technology that would eliminate the risk of contamination inherent in using fertile chicken eggs. 2 Big Pharma, by and large, has spurned the little biotech startups in San Diego, Austin, and Boston that have been searching for capital to develop exciting new recombinant and genetically engineered vaccines. In terms of vaccine development in general, the United States measures poorly even against tiny Cuba, which, thanks to the priority given to infectious and "poor people's" diseases, has become a world leader in creating state-of-the-art vaccines for meningitis B, Haemophilus influenzae, and other important infections ignored by giant drug companies in the United States. $\frac{3}{2}$ 

Meanwhile, aging and poorly maintained vaccine production facilities have been plagued by poor quality control and indifferent management. In September 2000, for example, 12 percent of the influenza vaccine supply was lost when the FDA shut down Parkdale Pharmaceuticals' contaminated facility, which never reopened; deliveries from Wyeth-Ayerst, which produced one-third of the national supply, were also delayed because of quality. By the winter of 2003-4—with the Institute of Medicine sternly warning Washington that the country was still "poorly prepared" for a flu pandemic—only two corporations were still making influenza vaccine for the U.S. market: Frenchowned Aventis-Pasteur with a manufacturing complex in Swiftwater, Pennsylvania, and Bay Area-based Chiron, with a recently acquired plant near Liverpool. 5

This was an extraordinary contrast to the situation in 1976, when *thirty-seven* companies in the United States produced flu vaccine, or for that matter, to current policy in the UK, where the government retains contracts with six major suppliers. Even as it hyped the importance of "biosecurity," the Bush administration in essence mortgaged the lives of tens of thousands of senior citizens, for whom annual influenza is a life-threatening illness, by relying on vaccine production in just two plants—and one of them, it would turn out, had an alarming record of poor quality control.

The 2003-4 flu season brought another vaccine disaster: a virulent strain of annual influenza (H3N2 Fujian), which

was not included in the vaccine mixture, proved more dangerous than expected to small children, and the old-fashioned egg-based production system precluded any last-minute reformulation of the vaccine. Even with a component missing, vaccine demand rose steeply; however, the two manufacturers, wary of being stuck with an excess supply as they had been the previous year, had manufactured too little, and some localities had to resort to rationing. While HHS had foreseen the likely shortfall, they had failed to exert enough pressure on the manufacturers to increase production.

As the media headlined stories about children in Texas. and Colorado dying from the Fujian strain, the CDC was nervously monitoring the new, extraordinarily widespread outbreak of H5N1 in Asia. Secretary Thompson finally acknowledged—although with less urgency than previous announcements about anthrax and smallpox— that a flu pandemic was an imminent danger, and the administration promised to accelerate vaccine development. Despite widespread criticism of their conduct during the previous flu season, Thompson decided to again make Aventis-Pasteur and Chiron the twin pillars of the U.S. vaccine program. In May both corporations received contracts from the National Institute of Allergy and Infectious Diseases to produce experimental lots of an H5N1 vaccine using a seed strain from Robert Webster's laboratory at St. Jude; in mid-August, Chiron was also awarded the contract to develop a vaccine against the H9N2 subtype.

In retrospect, it is hard to fathom Thompson's confidence in Chiron. Under a succession of previous

owners, its Liverpool plant had developed a notorious reputation for contamination. British authorities had once recalled contaminated polio vaccines made in the plant, while the FDA had admonished a previous owner about impurities in its flu vaccine. In the summer of 2003, FDA significant discovered risk of inspectors contamination in twenty different production activities, especially in the sterilization processes; because the plant was responsible for manufacturing almost half of the U.S. supply, the vaccine inspection team recommended compulsory steps to mitigate the danger. Their superiors, however, insisted upon voluntary, rather than mandatory, compliance. The agency then curiously delayed for nine months before forwarding Chiron its full inspection report, and, instead of sending inspectors back to monitor Chiron's progress, FDA officials consulted with the company by telephone or email.

In July 2004, Chiron found *Serratia marcescens*—a bacteria that can cause deadly septic shock—in several batches of vaccine. Instead of immediately alerting the FDA, the company instead issued a press release "boasting that it already had shipped 1 million doses of Fluviron vaccine to the U.S. market and planned to ship 52 million more doses." Chiron waited more than a month, until August 26, to notify the FDA of contamination. Once again, Crawford trusted the corporation to rectify the problem. At the end of September, Chiron CEO Howard Pien personally reassured the Senate Committee on Aging that quality control had been restored to the Liverpool plant, which would soon ship 48 million doses of vaccine to the United States; instead, a

week later, vigilant British inspectors shut the plant down and revoked Chiron's license to sell flu vaccine. Although the corporation claimed that a portion of the vaccine was uncontaminated, FDA investigators determined that the entire stock was spoiled.

As a result, the United States lost half of its seasonal vaccine and was forced to ration the rest. Although the CDC and local health officials worked miracles in shifting vaccine to areas of greatest need, the crazy quiltwork of the U.S. vaccine distribution system—with literally thousands of independent government and private agents involved—gave a disturbing foretaste of the chaos that a pandemic would create. The Chiron disaster easily risked killing as many Americans through lack of vaccination as the 9/11 attacks, but Thompson, Crawford, and their underlings continued to breezily disclaim any responsibility for errors of oversight. Amazingly they also let Chiron keep its contracts for manufacturing avian flu vaccines.

As public anger grew over the fiasco, which was soon followed by shocking exposes of the FDA's failure to monitor drug safety in a variety of cases, even the mainstream media was forced to acknowledge structural contradictions in the system. Thus, the *New York Times*, in a moment of almost Marxist revelation, identified the underlying problem as the "chronic mismatch of public health needs and private control of the production of vaccines and drugs." §

The vaccine crisis also prompted closer scrutiny of other major components of the pandemic plan, which in its snail's pace evolution since 1993 had finally arrived at the final comment and discussion phase in the fall of 2004. The *New York Times*—the only major newspaper that seemed to take avian flu seriously—published an editorial on October 12 chastising HHS for proposing to add only 2 million courses of oseltamivir (Tamiflu) to the Strategic National Stockpile. The editors pointed out that while Japan had purchased enough Tamiflu for 20 percent of its population, and Australia for 5 percent, the Bush administration's order would cover less than 1 percent of Americans. 9

In fact, there was gridlock in Switzerland, where Roche had failed to expand capacity to keep pace with its overflowing order book. The manufacturer recommended that governments stockpile enough Tamiflu to cover one-quarter of their populations, the estimated infection rate of an influenza pandemic; this rule of thumb would mandate 1.6 billion courses globally, with 74 million for the United States. Roche's recommendations might have been self-serving, but they were not far-fetched: Dr. Julie Gerberding, the head of the CDC, told the *New York Times* that she would like to see a U.S. stockpile closer to 100 million courses than 1 million. But in the fall of 2004, Roche, although it was trying to add a new production line, was only producing 8 million courses per year. 10

The obvious solution to both the Tamiflu shortage and the vaccine fiasco is for the federal government itself to undertake the nonprofit development and manufacture of lifeline medications. But in a political system where almost everyone dances to the tune of the drug industry's political contributions, the "liberal" alternative to the Bush administration's negligence was the proposal, supported by

presidential candidate John Kerry and other Democrats, to raise market demand with larger government purchases. Meanwhile, for the foreseeable future Americans would be trapped in precisely the dilemma that Robert Webster had warned about: How should the scarce supply of Tamiflu, the only antiviral known to be effective against avian influenza, be rationed? In late September, the Pentagon circulated its own pandemic planning guidelines which emphasized that the Tamiflu "supply is extremely limited world wide, and its use will be prioritized." Soldiers first, children last?

Michael Osterholm, the director of the University of Minnesota's Center for Infectious Disease Research and Policy, garnered much press attention with a warning that the H5N1 vaccine that the National Institutes of Health had developing with Aventis-Pasteur had immunogenicity" (ability to trigger an immune response). Osterholm warned: "The earlier versions of this vaccine are not protective against the current [H5N1] strains." He doubted that the government's slow-motion vaccine program would provide a safety net in advance of a pandemic. 12 Keiji Fukuda, the CDC's top flu epidemiolo-gist, direly predicted that at the beginning of a pandemic "there would be panic" and that hospitals would be unable to find room for all the acute cases. $\frac{13}{1}$ 

Similarly, in the aftermath of the vaccine fiasco, both the *Washington Post* and the nonprofit Trust for America's Health published devastating balance sheets revealing Project BioShield's failure to enhance the country's biological security. The *Post* reporters, who interviewed former administration officials, found that the "great

majority of U.S. hospitals and state and local public health agencies would be completely overwhelmed trying to carry out mass vaccinations." And indeed, during a May 2003 mock casualty exercise to test Chicago's capacity to cope with a bioterror attack or a pandemic, the emergency infrastructure collapsed. Richard A. Falkenrath, a former chief advisor on homeland security, told the *Post* that "the government's reliance on state and local health agencies to speedily distribute vaccines and drugs is the 'Achilles heel' of U.S. biodefenses." 14

The Trust for America's Health was equally pessimistic. One-third of states had cut back their public-health budgets in 2003–4, and a majority were woefully unprepared to undertake high biosecurity lab work, to distribute vaccines, or to track outbreaks. Although "most public health officials call the emergence of a new lethal strain of the flu 'an inevitability,'" only thirteen states had pandemic plans that met federal guidelines, while twenty states had failed to generate any plan. Earlier In February 2004, the Trust had warned that "pandemic flu could be much more demanding on state and local health resources and much more damaging to the general population than a bioterrorism attack." It predicted that a pandemic would "cripple the resources of a U.S. public health system already stretched too thin." <sup>15</sup>

Except for those lucky few—mainly doctors and soldiers—who might receive prophylactic treatment with Tamiflu, the Bush administration had left most Americans as vulnerable to the onslaught of a new flu pandemic as their grandparents or great-grandparents had been in 1918.

Pandemic planners admitted that the bulk of the public, initially at least, would simply have to cower in their homes. In a presidential election season dominated by "national security," pandemic vulnerability should have been a decisive wedge issue; however, the Kerry campaign scolded Bush for the vaccine debacle and promised to stabilize future production with government purchases of unused stocks, but otherwise offered few substantive ideas for repairing America's collapsing public-health infrastructure. 16

The only presidential candidate to pay attention to the monster at the door was Ralph Nader, the candidate whose presence in the campaign was so reviled by "progressive" born-again Democrats. In February 2004 Nader contrasted the administration's obsession with Irag's nonexistent "weapons of mass destruction" with its failure energetically address avian flu in Asia. "The chain of infections from domesticated Chinese ducks to pigs to humans," he forewarned in colorful prose, "can explode into a world war of mutant viruses taking millions of casualties before vaccines can be developed and deployed." Six months later, he wrote a public letter to Bush impeaching the administration's failure to act upon the warnings of top researchers and medical organizations. "Such notice apparently is not enough to move your Presidency to action. These mutating viruses are not like human villains. You need to recognize that their indiscriminate destruction of innocent civilians, however, can be considered a form of viral terrorism." In the WHO's "worst-case" scenario, 2 million of these "innocent civilians" threatened with death

are Americans, most of the remaining 98 million, however, live in the poor cities of the Third World.

# CHAPTER 10: THE TITANIC PARADIGM

Access to medicines has become the test above all others by which the rich world will be judged in its dealings with the poor. 1

Richard Horton

Scientific agreement about the imminent danger of an avian flu pandemic is almost as broad and all-encompassing as the consensus that humans are largely responsible for global warming. All the summit organizations responsible for world health, including the WHO and the CDC, have warned that the coming viral hurricane might be even more deadly than the 1918 pandemic. The major dissenter to this view is Amherst biologist Paul Ewald, a controversial advocate of "evolutionary medicine." In his view, the leading influenza experts have failed to grasp elementary principles of viral evolution, especially "the selective processes that favor increased or decreased virulence of virus strains." The 1918 pandemic, in his view, was a unique historical event whose catastrophic outcome depended upon the evolution of influenza virulence in the extraordinary conditions of the Western Front. "Both theory and the evidence," he claims, "implicate the Western Front as the source of the epidemic." Ewald doubts that environmental conditions so favorable to the emergence of hypervirulence in influenza A will ever reappear.<sup>2</sup>

Some scholars, of course, would dispute that the virulent second wave of the 1918 virus originated in France at all: Kansas, in fact, seems a better bet. Still, Ewald may be correct that crowded Army training camps, hospitals, and ships, as well as the trenches themselves, were the bellows that turned outbreak into conflagration. The 1918 pandemic dramatically grew in virulence between its initial spring outbreak and the deadly second wave in the early fall, so the key variables must have been crowded, often unsanitary conditions with large concentrations of sick victims able to transmit an evolving virus quickly to distant locations. Ewald calls such an environment a "disease factory." He might also have called it a slum.

The Western Front of the world's first industrialized war recapitulated much of the disease ecology of the classic Victorian slum—the *locus classicus* of most discourse about infectious disease. In the nineteenth century, the great slums of Europe, America, and Asia had a total population of perhaps 25 million; today, according to UN-Habitat, there are 1 billion slum dwellers: a number expected to double by 2020. Is there any reason to assume that today's bustees, colonias, and shantytowns are any less efficient "disease factories" than Victorian slums or crowded 1918 army camps? If, according to Ewald, the *sine qua non* of a deadly airborne pandemic is "host density" in poor sanitary conditions, then today's megaslums are just as fetid and any of their overcrowded notorious Victorian as predecessors.

To recapitulate from earlier chapters, the two global changes that have most favored the accelerated crossspecies evolution of novel influenza subtypes and their global transmission have been the Livestock Revolution of the 1980s and '90s (part of the larger world conquest of agriculture by large-scale agro-capitalism) industrial revolution in South China (the historical crucible of human influenzas), which has exponentially increased the region's commercial and human intercourse with the rest of the world. The emergence of Third World "supercities" and their slums, then, would constitute a third global condition tantamount to Ewald's Western Front as a human medium for potential pandemic spread and virulence evolution. But there is also a fourth, negative element that closes the ominous circle of influenza ecology: the absence of an international public-health system corresponding to the scale and impact of economic globalization. Such a system, as Laurie Garrett emphasizes in her much-praised book, Betrayal of Trust: The Collapse of Global Public Health, "would have to embrace not just the essential elements of disease prevention and surveillance that were present in wealthy pockets of the planet during the twentieth century, but also new strategies and tactics capable of addressing global challenges." Nothing like this, of course, now exists, and Garrett paints a dark, almost despairing portrait of how the worldwide HMO revolution has promoted costcontainment at the expense of saving lives.

Richard Horton, the editor of *The Lancet*, the premier British medical journal, offers an equally bleak view of world public health. "UNICEF and WHO have largely

abandoned the world's children to die in poverty. For example, spending on immunization by UNICEF totaled \$180 million in 1990. By 1998, the figure had fallen to around \$50 million." Some 11 million children under the age of five die each year, and "99 per cent of these deaths occur in setting of acute poverty." Horton accuses the WHO, even under the supposedly enlightened tenure of Director-General Gro Harlem Brundtland, both of being subservient to corporate elites and "of censorship when criticism was made of the pharmaceutical industry." He also damns the Bush administration's sordid crusade to defend Big Pharma's monopoly over drugs treating chronic conditions. "Once again," he wrote after a 2002 U.S. veto of Third World efforts to obtain cheaper generic pharmaceuticals, "access to vital drugs to treat health emergencies among those living in poverty will be restricted solely to protect profit. And WHO has nothing to say on this issue."5

Many Third World governments, meanwhile, are disinclined to spend much on public health when the alternative is feeding their generals' bottomless appetites for new weapons. Delhi, for instance, spends 16 percent of its budget on defense, but only 2 percent (\$4 per capita per annum) on health. Other poor countries are too shackled by structural adjustment and debt to have any choice. "Kenya," Alex de Waal complains, "finds itself unable to offer jobs to several thousand unemployed nurses because of a cap on public-sector employment, while Zambia is in the extraordinary position of being required to lay off health-sector employees, even while many districts have no health professionals at all." In sub-Saharan Africa, where

100,000 trained medical workers were lost during the 1990s to AIDS or emigration, it is estimated that the region desperately needs at least 1 million more personnel, especially nurses and assistants, to ensure even the most rudimentary public-health coverage to the entire population.<sup>8</sup>

In the face of the peril of avian influenza, as with HIV/AIDS earlier, world public-health resources are organized rather like the lifeboats were on the Titanic: many of the first-class passengers and even some of the crew will drown because of the company's skinflint lack of foresight; the poor Paddies in steerage, however, do not even have a single lifeboat between them, and thus, they are all doomed to swim in the icy waters.

Only twelve drug companies make influenza vaccines, and fully 95 percent of their output (about 260 million doses) is consumed in the world's wealthiest countries. Current production is limited by the supply of fertile eggs, and even a switch to cell culture—as all experts advocate would face the problem that "there are surprisingly few suitable accredited cell lines and cell banks available, and many of those are the property of pharmaceutical companies." Despite the WHO's urgent Geneva summit in October to lobby governments to finance (and drug companies to produce) a so-called "world vaccine," little progress has been made. "Of the world's major flu vaccine manufacturers," Science reported during the summit, "so far only two are willing to tackle the financial, regulatory and patent issues involved in making a new pandemic vaccine, mainly for the U.S. market." Previous test

vaccines, as we have seen, failed to keep pace with the evolving virulence of H5N1, and even if current clinical trials are successful, Washington has ordered only 2 million doses from Aventis-Pasteur. With the exception of Canada (which has contracted with a Quebec-based firm to gear up production for 6 million doses per month), most wealthy countries are buying just a few "lifeboats" now in the dubious belief that they will have time to order more when the crisis arrives. <sup>11</sup>

Without vaccines, as we have seen, there will be a mad global scramble over Tamiflu: according to Science, "the world's only initial defense against a pandemic that could kill millions." 12 Back in 1999, René Snacken, the chair of the European Scientific Working Group on Influenza, warned that "waiting until a pandemic strikes to determine access to prophylactic materials inevitably contributes to inequities in supply for countries to produce antiviral agents or vaccines or lacking resources to competitively purchase supplies at a time of scarcity." 13 The WHO, of course, has stressed the "need for international solidarity"; arguing that the only way to contain an initial pandemic outbreak will be to douse it with powerful antivirals. It has urged the pooling of Tamiflu for use in Southeast Asia. "But whether countries will voluntarily ship their own precious stockpiles overseas to fight a faraway plague remains to be seen." Even if some antivirals are made available, there is little guarantee they will actually reach people in the hot spots.

But this appalling lack of vaccine and antivirals is not the only problem faced by the global "steerage class." The death tolls during the 1957 and 1968 pandemics were dramatically reduced by the widespread availability of new, secondary effective antibiotics to treat pneumonias—but the major bacterial pathogens, including the pneumococci and *H. influenzae*, have evolved resistance to penicillins, erythromycin and other antibiotics usually employed in hospitals. Such a cycle of resistance is the inevitable result of natural selection, and the only solution is the constant development of new antimicrobial therapies, but the pharmaceutical industry has largely abandoned antibiotic research (although it sells huge quantities of antibiotics to the livestock industry and thus contributes to the accelerated obsolescence of the current generation of antibiotics). In the event of a pandemic, there is a great risk that mortality from bacterial pneumonia, especially in poor countries with limited supplies of older antibiotics, might return to pre-World War II levels.

How would almost defenseless Third World cities respond to a pandemic? The precedent that scares many public-health experts was the September 1994 outbreak of pneumonic plague in Surat, India's twelfth-largest city. Laurie Garrett and, at greater length, Ghanshyam Shah have both discussed the Surat experience "as a warning of epidemics to come." A city of textile and diamond-cutting sweatshops and slums with one toilet for every 150 people, Surat epitomized the polarized condition of urban health care in most of the Third World: a small modern sector existed for the affluent, and a wretched mixture of inadequate public medicine and sheer quacksterism sufficed for the rest of the population.

Shah describes a "public health system [that] has not only gone downhill in its delivery system but also lost credibility. Even the poor do not trust it." Although Surat had no shortage of doctors, most of them were in private practice, "motivated by a quick profit. Ethical values among medical professionals are disappearing very fast." 15 As patients began to present plague symptoms, the doctors were the first to flee the plague. "They were totally unprepared for what followed. The private doctors panicked. Eighty percent of them fled the city, closing their clinics and hospitals and abandoning their patients. The fear in those physicians' eyes did not go unnoticed by the populace, and rumors of a great impending disaster spread swiftly among the largely illiterate masses. Surat's middle class discreetly packed their bags and slipped out of town."16

Within days, wild rumors had overrun India, antibiotic stocks had been depleted, and Delhi had been forced to send the elite Army Rapid Action Force to guarantine Surat's slum dwellers from fleeing in the footsteps of the middle classes. The outside world, meanwhile, began to quarantine India, screening Indian jets or banning flights altogether; the Gulf states even stopped communications with the subcontinent. "WHO." Garrett writes, "did little to slow the [international] stampede toward hysteria or to stifle the opportunistic shouts of boycott." India appealed for international assistance, but few countries had inventories of plague vaccine, and new production would take six months. 17

Fortunately, the plague was contained in a week: "For many ... a miracle," writes Shah. Experts debate whether the massive application of antibiotics (tetracycline and chloramphenicol) was decisive or whether the plague bacterium simply became less virulent through evolutionary modification. Nonetheless, the immediate explosion of panic, the desertion of private doctors, the hoarding of antibiotics, the absolute lack of confidence in government, the use of force to quarantine the poor, the silence of WHO director-general Dr. Hiroshi Nakajima, and the hysterical stigmatization of India by its other countries—all confirmed experts' worse fears about the vicious circle of epidemic disease, slum poverty, and neoliberal politics. An influenza pandemic would magnify the Surat experience perhaps a hundredfold.

The WHO is most worried about Africa. "Without a doubt, the virus will get there," Klaus Stohr told *Science* in October 2004. "The situation will be much, much worse than anywhere else. Access to vaccines will not be an option, let alone antivirals." The 27 million or more Africans who are HIV positive, of course, would be the human bull's-eye of a H5N1 pandemic. "People with HIV/AIDS," says a CDC fact sheet, "are considered at increased risk from serious influenza-related complications. Studies have shown an increased risk for heart- and lung-related hospitalizations in people infected with HIV during influenza season ... and a higher risk of influenza-related death." AIDS, in other words, might become influenza's deadly dancing partner like malnutrition in India or malaria in Iran in 1918; as a result, the potential death toll could be

a full order of magnitude higher than the estimated 2 million Africans killed by the 1918 pandemic. Yet, apart from some public notice taken in South Africa, the continent is wholly unprepared to address a pandemic; many countries do not even return influenza questionnaires to the WHO. (In many cases, public-health systems have simply collapsed under the relentless weight of AIDS and civil war.) World indifference toward the AIDS holocaust in Africa, moreover, provides a lamentable template for current global inaction in the face of the avian influenza threat.

# CONCLUSION: YEAR OF THE ROOSTER

We're living on borrowed time.

Klaus Stohr (WHO) $\frac{1}{2}$ 

Alas, a flu pandemic is not a fate we can avoid. To recapitulate an earlier argument: Third World urbanization Livestock Revolution the and have fundamentally transformed influenza ecology and accelerated evolution of novel recombinants. Moreover, there are multiple pathways to a new catastrophe on the scale of 1918. As we have seen, several subtypes of H7 and H9, in addition to H5N1, are slouching toward Bethlehem with bright prospects of producing pandemic offspring. All the major candidates, in addition, appear to be increasing their evolutionary fitness to spread rapidly through new avian and mammal species. The fifteen HPAI outbreaks since 2000, for example, have killed or led to the culling of ten times as many birds as all earlier known outbreaks combined. ("We've gone from a few snowflakes to an avalanche," an Italian researcher told Science.)<sup>2</sup> Even if humanity miraculously dodged H5N1, we would soon be under threat from other virulent avian subtypes.

The rich countries have had nearly a decade—a unique advance warning in the history of disease—to build a

network of global defenses against the impending pandemic. But the crash program of vaccine development and antiviral stockpiling, advocated by Robert Webster and others since 1997, has yet to really commence. In Washington, London, and Tokyo, health ministers pay religious deference to pharmaceutical industry patents and profits while failing to assure the elementary provision of lifeline medicines. In Asia, as well as California and British Columbia, governments have covered up outbreaks, lied to international agencies, threatened whistleblowers, and possibly concealed illnesses and deaths. The huge livestock multinationals, with their crony ties to government in Thailand and China, have exploited the crisis to restructure poultry production to their selfish advantage. Although individual foreign researchers and institutions provided heroic assistance to local authorities, the overall global aid effort has been a disgrace. Most egregiously, the United States— the country with the greatest historical moral obligation to Vietnam—has failed to provide that poor nation with the resources to monitor or contain the outbreak.

Over the recent past, to be sure, some progress has finally been made on the vaccine and antiviral fronts. But the chief beneficiaries are a handful of wealthy countries—especially Canada, Australia, New Zealand, Singapore, and Japan—who have been provident enough to order early and in quantity from Roche. Britain, France, and Sweden have also taken serious steps, but the United States, which has recently spent billions on "biosecurity," lags shockingly far behind its peers. We are better equipped to deal with

imaginary anthrax and Ebola attacks than with an avian influenza pandemic. Meanwhile not the slightest effort has been made to protect the truly poor countries of Asia and Africa from the return of history's greatest killer. A "global vaccine" is still a pipedream, and the Tamiflu buying spree by the rich countries has locked up the potential supply.

As with HIV/AIDS and the easily preventable infant diarrhoeal diseases, avian influenza is a fundamental test of human solidarity. Access to lifeline medicines, including vaccines, antibiotics, and antivirals, should be a human right, universally available at no cost. If markets can't provide incentives to cheaply produce such drugs, then governments and Nonprofits should take responsibility for their manufacture and distribution. The survival of the poor must at all times be accounted a higher priority than the profits of Big Pharma. Likewise, the creation of a truly global public-health infrastructure has become a project of literally life-and-death urgency for the rich countries as well as the poor. The first step—as the editors of *Nature, The* Lancet, and other eminent journals have repeatedly emphasized—is a serious aid program to rescue the antipandemic campaign in Vietnam and Southeast Asia. On the thirtieth anniversary of the end of its genocidal intervention in Indochina, the United States needs to help the small farmers of Vietnam save the lives of their children.

As the hour hand on the pandemic clock ominously approaches midnight, I recall those 1950s sci-fi thrillers of my childhood in which an alien menace or atomic monster threatened humanity. Scientists try to sound the alarm, but politicians ignore the danger. Ultimately, however, the

world wakes up to the peril and unites to defeat the invader. Human species survival overrides the antagonisms of the Cold War and competitive nationalism. Now, with a real Monster at our door—as terrible as any in science fiction—will we wake up in time?

# **NOTES**

#### INTRODUCTION

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## **CONCLUSION**

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